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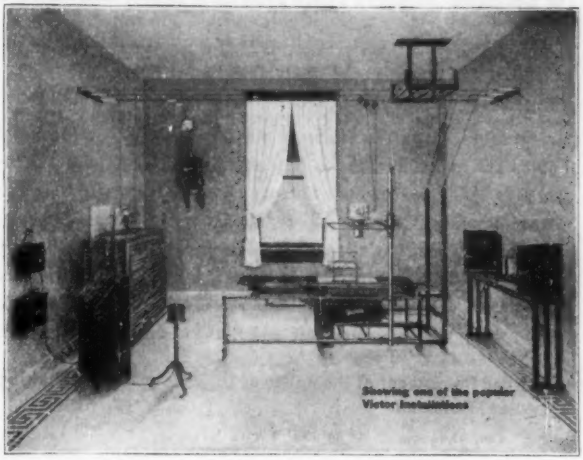

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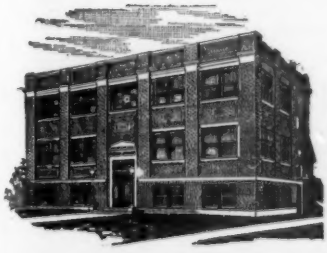

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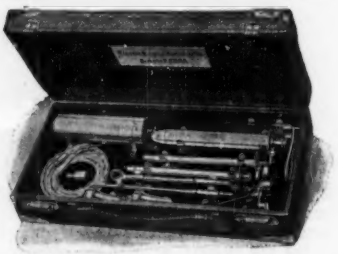

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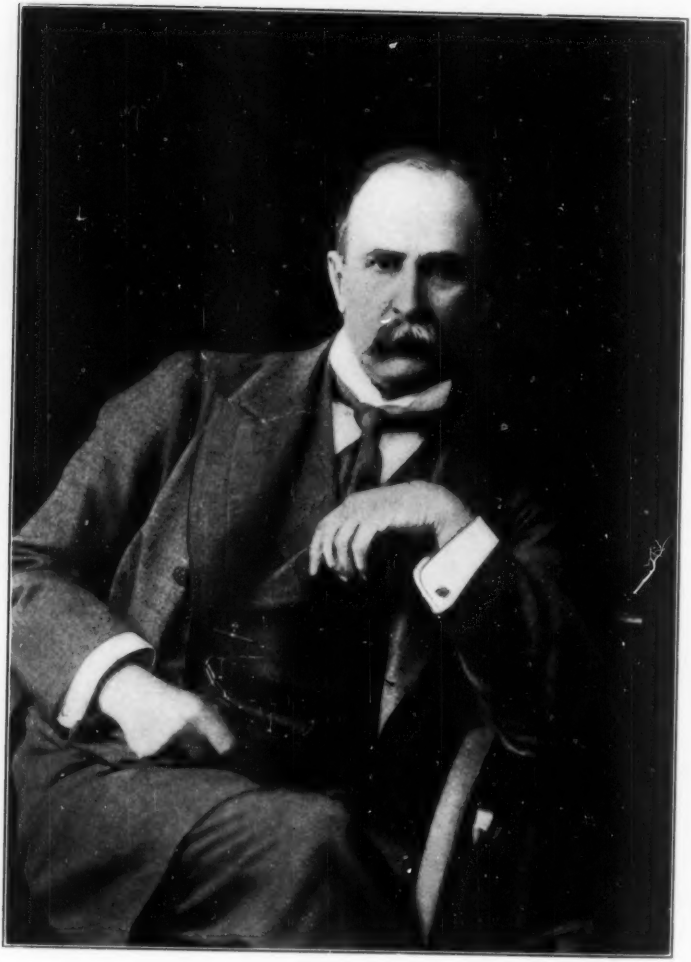

W. Osler

WILLIAM OSLER.

A GREAT physician, a wise counsellor, a true man and above all a friend has gone to his long home. William Osler is dead. There is no man in the profession in any land whose passing could bring sorrow and a keen sense of personal loss to so many. It is a far cry from the rectory in Tecumseth, Ontario, in 1849, to Oxford in 1919; but the journey never seemed long to him, for he travelled cheerfully, did each day's work as it came and never lost a chance of helping others. His philosophy of life was simple—to do the day's work well and not trouble about the morrow, to act the Golden Rule and to cultivate a spirit of equanimity. Many other qualities were evident in his daily life; two stand out, kindness and the habit of charity toward all men. His darkest days came when his son gave his life in France, but he bore the sorrow with fortitude and kept on with his daily work—"Carry on" was the word. His work during the war was very heavy, and he was constantly laboring to the limit of his strength.

How can one state his many activities in a few words? Professionally he did much to advance knowledge, to improve medical education and to uphold the best traditions of a profession which he loved. A friend of young men, he never missed the opportunity to encourage and help them. How often he sent an approving word about an article or a good piece of work. As a teacher he did much to help medical education in this country and taught the lesson that the knowledge of disease is to be learned at the bedside rather than in the lecture room. A lover of books, he gave the first stimulus to many of an interest in literature, and especially in medical history. As a physician he inspired confidence and gave courage to the sick with a constant example of kindness and consideration to those about him.

He put his mark on medicine and men wherever he lived and worked. There are men in Philadelphia who show the influence of his teaching there over thirty years ago. Much of the success of the Johns Hopkins Hospital and Medical School is due to him. To the profession he gave freely of time and advice. His influence was always exerted to promote "Unity, Peace and Concord." For him the general practitioner was the backbone of the profession. He would never listen to any word said in detraction of a brother practitioner.

There were other activities. His knowledge of literature was extensive and in him the Greek philosophers had an eager student. For one without a special training his classical knowledge was remarkable. His essays take no mean place both in matter and style. But after all, what we think of most is the humanness of the man—"Homo sum; humani nihil a me alienum puto." He met the ignorant and the wise and both could learn from him. That he did so much was a constant wonder, but he knew the value of minutes and had the art of concentration. Of his kindness to others one learned only by chance; many of the readers of this know of his kindness to them.

Cheerfulness was a characteristic; work with him was never dull. He never had to unbend, and where he sat was the head of the table. What a fund of reminiscence and incident he had and how naturally and easily he could draw on it. The opportunity for a jest was rarely lost, but the jest was a kindly one. A wound was rarely felt by the one at whom the arrow was shot. But how his lighter doings and sayings puzzled some of his acquaintances—not his friends, for they understood.

To those who worked with him in Baltimore many memories come back of the days in the hospital and classroom. No man ever had more devoted assistants; to them he was "The Chief," and that title in their thoughts can never belong to anyone else in the sense that it did to him. The alert, active figure entering the hospital a few minutes before nine, and always on time, the ward rounds, the hunt in the library for an article, the discussion of some special point, the interest of the clinic, are part of the recollections that come back. For his students the Saturday evenings at his home must stand out as perhaps the best hours of their undergraduate life.

Now we have the memories only, but they are precious ones. For many of us William Osler stands as the strongest influence in our lives. He will be missed and mourned, but his influence goes on and generations of medical students yet unborn will profit by his life and work. From his passing there will be for many an added meaning to the words of Milton:

> But O the heavy change, now thou art gone,
> Now thou art gone, and never must return!

THOMAS MCCRAE.

THE CENTENNIAL OF THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES

With the present number the American Journal of the Medical Sciences completes one hundred years of uninterrupted existence. For any periodical, especially one devoted exclusively to a technical subject, such as the science of medicine, to have withstood successfully the vicissitudes of a century, is an achievement to which both the publishers and editors may point with pardonable pride. Throughout all these years not only has the American Journal enjoyed continuous publication, in spite of recurring alternations of peace and war, but during this time its record of accomplishment has been great and its influence upon the development of American medicine has been undeniable.

Since its first volume appeared, under the editorship of the celebrated Dr. Nathaniel Chapman, up to the present the Journal has consistently upheld all that is highest and best in medical tradition. It has striven always to place before its readers the progressive and scientific without neglecting the practical importance of the art of medicine. The late Sir William Osler once referred to the American Journal as "One of the few great journals of the world." That this assertion was amply justified becomes evident when one considers that successive generations of leading medical writers have contributed freely to its volumes epoch-making articles, many of which will ever stand as milestones along the road of American medical progress. The Journal has been instrumental in molding medical thought not only here but also abroad, for being, with one exception, the oldest medical periodical in the English language it has been able to play a leading role in bringing before the profession of other lands the medical contributions of this country.

Those who today guide the destinies of the American Journal are keenly aware of the heritage that is theirs and the responsibilities that it entails. It will ever be their earnest endeavor to maintain the high ideals in medical journalism for which this publication

has so long been conspicuous. It is their intention to commemorate this one hundredth anniversary of the JOURNAL not by a single number of unusual merit, but rather by making every issue that appears in 1920 noteworthy for the exceptional value of the contributions it contains. They aim to make the JOURNAL of the future the same honest, scientific, helpful periodical that it has been in the past. In this way they hope that during the years to come the AMERICAN JOURNAL will continue to deserve the confidence and support of the medical profession, a factor that has contributed so largely to its success during the past one hundred years.

G. M. P.

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ORIGINAL ARTICLES

SOME PRACTICAL POINTS IN PROSTATIC SURGERY.[1]

By John B. Deaver, M.D.,

PHILADELPHIA.

The mortality rate following prostatectomy is in direct ratio to three vitally important factors: (1) The recognition of absolute contra-indications to operation; (2) the recognition of relative contra-indications to operation, and (3) the knowledge of methods of treatment preliminary to operation that will remove such relative operative contra-indications and thus bring the individual within the operable class.

Characteristic illustrations of these factors are most frequently found in subnormal function of the kidneys. In one instance an impending uremia may be due solely to an antecedent nephritis of the chronic interstitial type, in which event, the cause being irremovable, there is an absolute contra-indication to operation. In another instance a minor degree of interstitial nephritis may exist, but the dangerously low renal function present is dependent upon back pressure incident to lower urinary obstruction. Under these circumstances there is a relative contra-indication to operation, because after decompression of the kidneys the renal function improves, so that eventually the obstructing prostate can be removed successfully.

Similar relative contra-indications occur as the result of altered kidney function, consequent upon decompensation of the cardio-

[1] Read before the Buffalo Academy of Medicine, Buffalo, N. Y., November 5, 1919.

vasomotor systems. With proper treatment the blood-vascular tone may improve and coincident with it the renal function is restored. Such restoration of function could obviously be accomplished in no other way in cases of this kind than by treatment of the cardiovascular system.

In a small proportion of cases an obviously enlarged prostate may be accused of giving rise to symptoms and conditions for which it is only partially or even not at all responsible. Mistaken diagnoses of this kind are almost invariably due to lack of completeness in the physical examination, and especially of the nervous system. In an individual with early tabes and an enlarged prostate gland the symptoms of prostatism may be due chiefly to bladder atony resulting from the cord lesion. This constitutes an absolute contra-indication to prostatectomy. In other instances removal of the prostate is indicated, but only after it has been definitely established that the symptoms are due in major part to its enlargement. The tabetic lesion constitutes a relative contra-indication, in that specific treatment is advisable before removal of the prostate is attempted. In many instances the differentiation between absolute and relative contra-indications is a most difficult, if not impossible, matter. We cannot reproach ourselves for the mortality following prostatectomy in those cases in which every attempt has been made to make this differentiation, but in which the contra-indications which seem to be relative were, as events proved, absolute once.

In only a small proportion of cases does the primary examination reveal complications that absolutely preclude the possibility of operation. The majority of complicating factors that would result in a fatality with immediate operation are so far removable that prostatectomy can be performed later in comparative safety. The success of the individual surgeon is far more dependent upon his ability to recognize and treat relative contra-indications, together with the selection of the proper time for operation, than upon his technical skill in removing the obstruction.

The general mortality rate of prostatectomy throughout the country is well above 20 per cent., and 69 per cent. of all deaths following the operation are caused by uremia, hemorrhage, shock and sepsis. In a collected series of 147 cases of the immediate postoperative death, uremia was given as the result in 39 instances, hemorrhage in 32, shock in 18 and sepsis in 13. Practically the same mortality rate is attributable to uremia and sepsis as is given for hemorrhage and shock. In other words, about half of the operative mortality dependent upon the major causes of operative death follow complications that existed as relative contra-indications before operation; the remaining deaths are directly dependent upon technical complications of the operation. If we include other causes of death, such as asthenia, infected kidney, etc., with the group that presented preoperative contra-indications, the percentage of deaths due to

failure to recognize the danger signals will be materially increased. It is difficult to realize that almost as many prostatectomy deaths are due to hemorrhage as to uremia, but such is the fact. It is necessary to recognize and to treat properly the relative contra-indications to prostatectomy and to so perform the operation that fatal hemorrhage and sepsis will be rare events, instead of the extraordinarily common ones which they are at the present time if the mortality of prostatectomy is to be reduced.

Absolute contra-indications to the removal of the benign hypertrophic prostate are frequently encountered; that they are too often disregarded is evident from the existing mortality rate. The relative contra-indications are presented in the vast majority of cases; here, again, the high mortality rate bespeaks the indifference of many operators to dangerously low functional activity of vital organs. One of the rarely admitted absolute contra-indications to operation is the inability of the surgeon to control hermorrhage or to remove the prostate within limits of traumatic injury that the patient is able to bear.

The absolute organic contra-indications generally affect groups of organs rather than a single organ, although the major symptomatology will often direct attention, especially to one or other organ or system. An exceedingly high blood-pressure, for instance, in an aged individual is usually indicative of cardio-arterial pathology, but in some instances it is largely compensatory to interstitial nephritis. When purely compensatory in type a failure in compensation may occur after prostatectomy, owing to the added strain thrown upon the kidneys. Nature may fail in her attempts to further increase the blood-pressure so as to insure renal function, or, having successfully accomplished this, a cerebral vessel may burst or the heart may suddenly dilate, with death following in either event. In the absence of these fatal factors death may occur from renal failure, notwithstanding a better cardiovascular function after operation than before. High arterial tension in itself is not a positive contra-indication to operation, but a cardiovascular system which shows no elasticity in function after the institution of treatment designed to relieve the causes of high arterial tension is not dependable, and if, in spite of the maximum compensatory activity of the cardiovascular system the renal function, despite treatment, is barely sufficient it is worse than foolhardy to attempt prostatectomy. A decompensated cardiovascular system which does not respond to treatment obviously contra-indicates operation. Impending uremia commonly delays operation but does not necessarily preclude it. We are realizing more and more how really few prostatics have kidney defects which cannot be removed or at least relieved sufficiently to make the individual safe for prostatectomy.

In our experience sepsis and toxemia productive of a general low ebb vitality are frequent contra-indications to operation. In these

cases a low-grade uremia is often a chief contributing factor, but this is not always true. We refer now to the individual prematurely aged as the result of excesses, the victim of manifold chronic toxemias whose vitality is further sapped by chronic sepsis of bladder and kidney origin. These individuals are anemic, their tissues are flabby, their appetite is poor and their resistance nil. The renal function in this class of patients may be relatively normal and the most careful examination may fail to reveal any positive contra-indication to operation; yet we know from experience that these patients die after prostatectomy from causes that are grouped under the term asthenia. After weeks or months of the most careful treatment many of these patients can be safely operated upon; to operate them without such preliminary treatment is inexcusable.

Renal failure is by far the commonest contra-indication to operation, but it is usually a relative contra-indication. It is our duty to determine the degree of renal impairment and the possibilities of its improvement under treatment. The surgeon must familiarize himself with the various methods of measuring renal function and of selecting and applying methods of treatment best suited to restore this function, and, finally, he must be able to recognize maximum renal function and to judge correctly the ability or inability of the kidneys to support life after prostatectomy. Surgical success in these cases, above all others, depends upon the abilities of the surgeon as a physiologist.

We are fortunate in having many means of estimating renal function—our misfortune lies in not possessing any other method that will accurately measure the function of the kidneys in every instance. It is only by repeated examinations and weighing the evidence furnished by many tests that one can accurately gauge kidney function, especially as regards the reserve capacity of these organs. The tests of retention, of which the most important is the blood-urea test and the tests of excretion, of which phenolphthalein is the most accurate, usually give similar results. This is by no means the invariable rule, however, and on account of these exceptions the tests of excretion are sometimes condemned. To condemn these or any other tests because of exceptional failures is unfortunate, inasmuch as they are capable, when properly interpreted, of giving much valuable information. It is likewise a mistake to pass one's opinion on a single test, inasmuch as the tests of excretion are indicative only of the function of the kidneys during a specific interval of time. A single test of retention is more to be relied upon than a single test of excretion. Urea in the blood is the ash of protein derivatives and in the absence of tissue obstruction is derived almost entirely from the food. Furthermore, it is a threshold substance which is taken from the blood by the kidneys when the normal concentration is exceeded. Therefore, renal failure promptly gives rise to urea retention. This rule, too, is not

without exceptions, and in certain instances an impending uremia may exist though the blood urea is only slightly if at all increased.

A concentration of urea, 0.5 gm., and of the total incoaguable nitrogen, 0.6 gm. per liter of blood, has been the accepted normal level, but Folin and Davis have found that a concentration of non-protein nitrogen 26 mg. and urea nitrogen 13 mg. per 100 gm. of blood is normal. Concentrations of less than 0.6 gm. of urea per liter of blood are of little prognostic significance in our experience. The results of the blood-urea test are always contrasted with the phthalein excretion. A low phthalein output, 20 per cent. or less, is usually but not always associated with retention of urea. If a low phthalein excretion and urea retention occur together the renal function is certainly greatly impaired; operation should be withheld until these results are confirmed or disapproved by repeated tests. If, on the other hand, a low phthalein output is not associated with urea retention and the general condition of the patient is good, we are prone to disregard the results of the phthalein test. Again. a high percentage output of phthalein is not incompatible with dangerous urea retention. These are exceptional cases, however, and they are certainly not good reasons for discarding so valuable a procedure as the phthalein test. We are prone to forget the old-time tests of renal function. Their very simplicity no doubt condemns them to forgetfulness. I refer to the quantity of the urine and to its specific gravity. As a rule the results of the kidney function tests indicate an altered state of function which Nature has expressed in the production of a urine low in content of solids, and therefore low in specific gravity, but often great in quantity. We have, however, seen cases in which the various functional tests indicated a good state of renal function but in which the urine was abnormally low in specific gravity. I personally would refuse operation in any individual whose urine showed a specific gravity persistently below 1005, regardless of the results of any functional tests. No fear of uremia need be entertained for the individual whose kidneys secrete a normal quantity of approximately normal urine. The quantity of urea in the urine is of little prognostic significance, except it be compared with the quantity of blood urea; we believe that Ambard's constant is of value and should be taken advantage of in clinics where laboratory facilities are at hand for its estimation. It is important that the urine be studied for acetone and diacetic acid. Acidosis is a factor to be reckoned with therefore every precaution to prevent as well as to correct it when it occurs.

Cultures of the urine are made in all our prostatic cases, since we believe it is important to know the type of infecting microörganisms present. This enables us to intelligently guide the preoperative treatment, especially as regards the length of time necessary to continue preliminary drainage of the bladder. It is also of assistance in determining whether preliminary cystostomy should be done,

and if so, what type of local treatment is to be employed and how long it should be continued. Sensitized bacterins are occasionally of value in helping to overcome the infection, especially in the presence of a complicating pyelitis.

Practically all of our patients are cystoscoped, but not until they are subjected to preliminary treatment. The bowels should be freely opened with a saline cathartic. Copious drinking of water should be encouraged and formin and acid sodium phosphate administered for several days at least before the cystoscopic examination is made. The cystoscopy is absolutely essential in certain cases of hematuria for the differential diagnosis of benign from malignant prostate or in the recognition of a complicating papilloma. The size and shape of the intravesical portion of the prostate is determined cystoscopically as well as bladder complications, such as stone and diverticulum. Vesical diverticulæ are important causes of morbidity following prostatectomy. A pouch of this nature in communication with the bladder cavity will give rise to the symptoms of prostatism, and if the patient is informed of the probable necessity of a second operation for its removal the surgeon will be spared much embarrassment when the removal of the prostate fails to remove the symptoms.

Low renal function in prostatics is not infrequently dependent upon surgical kidney, so that differential studies of kidney function are sometimes necessary. In these cases we prefer the indigocarmine test. This test is particularly applicable to prostatic cases on account of the ease and rapidity with which it may be performed.

Catheterization of the ureters, which is often difficult and sometimes impossible in the presence of large intravesical projections, is unnecessary. Obviously this test lacks the exactness and refinement of differential phthalein studies, but it serves for all practical purposes in prostatic cases in which differential studies are necessary.

Preliminary Treatment. Practically all prostatics are in need of treatment before operation can be safely undertaken. In certain cases of acute retention, prolonged and unsuccessful attempts to insert a catheter have so traumatized the urethra that further attempts to relieve the patient instrumentally are unjustified. Under these circumstances the bladder should be drained suprapubically. The bladder may be explored with the finger at this time and any calculi should be removed. In desperate cases in which the retention has continued for a long time and the bladder has become greatly overdistended the sudden relief of intravesical pressure is extremely dangerous. Formerly we employed the trocar in cases of this kind, but probably a better procedure is the introduction, under local anesthesia, of a female retention catheter. The bladder is exposed suprapubically, the bulb of the cathether is

folded and grasped in the jaws of a pair of dressing forceps and is introduced through a very small incision into the bladder. The tube is clamped off and traction is put upon it so that the bulb of the catheter fits snugly against the bladder mucosa. If too large a single stitch will serve to close the incision tightly around the catheter. This procedure can be carried out with the loss of little if any urine. By removing the clamp from the tube at intervals the bladder may be emptied intermittently. This does away with great danger, due to sudden and complete emptying of the bladder. Under ordinary circumstances we prefer a drainage tube of large caliber, but in cases of long-continued complete retention which cannot be relieved *per urethram* I am sure that the above procedure is a life-saving measure. Long-continued drainage of the bladder, which is usually necessary in these cases, can be accomplished in this manner most effectively and without discomfort to the patient incident to the prolonged leakage of urine. This is the only type of case in which it is necessary to operate immediately, and primary prostatectomy is attended by approximately 100 per cent. mortality in this group.

If the urethra is patulous we prefer the indwelling catheter in the initial stages of treatment in most cases, but under other circumstances, preliminary cystostomy should be performed without delay.

In draining the bladder suprapubically, as the first stage of a two-stage prostatectomy, we prefer, as we have just mentioned, a drainage tube of large caliber. This is especially indicated when cystitis is a prominent complication. Prolonged drainage is essentially necessary in cases in which extensive ecchymosis of the bladder mucosa has occurred. This condition is easily recognized by the chocolate-coated appearance of the mucous membrane, an appearance which is due to intramucosal and submucosal hemorrhages. The bleeding is the result of the local action of bacterial toxins. The mucosa becomes softened, thickened and irregularly stained by reduction substances derived from the hemoglobin, which give to the membrane its chocolate-coated appearance. This condition may, but rarely does, give rise to hematuria. The altered mucosa is much more absorbative than is the normal mucous membrane of the bladder, which fact explains the chronic toxemia from which these patients suffer. In this fact also we find the *rationale* for drainage of the bladder for a sufficient period to permit regeneration of the mucosa to take place.

Preliminary cystostomy, more than any other single procedure, has materially reduced the operative mortality of prostatectomy. We do not employ it routinely, however. In early cases of prostatic enlargement, that is, in patients with small amounts of residual urine, patients whose kidneys are functionally satisfactory and in whom there are no definite contra-indications to operation we prefer to remove the prostate without preliminary drainage of the

bladder. In the majority of cases the catheter is used either intermittently or constantly, and if the kidney function and general condition improve sufficiently, we proceed at once with the prostatectomy. In the remaining group of cases, which includes all those in whom the preliminary catheter treatment has failed, we advocate the two-stage operation.

There are certain technical difficulties associated with the removal of the prostate, which are dependent upon preliminary drainage of the bladder—difficulties which cannot easily be overcome. The size of the incision is limited to the distance between the drainage opening and the pubic bone, since it is unsafe to enlarge this incision upward on account of the danger of opening the peritoneal cavity, the peritoneum having become attached to the bladder wall in the line of the original incision. This gives insufficient exposure of the prostatic bed, and in the event of hemorrhage it is often difficult to apply gauze packing. This is the one certain way to control hemorrhage after prostatectomy. Distensible bags and similar playthings are effective only in cases in which there is no bleeding.

Very large prostates are usually easily enucleable, but it is frequently quite difficult to deliver them through the small suprapubic wound; in fact, it is frequently necessary to section the gland and remove it piecemeal.

Preliminary drainage of the bladder serves, however, to relieve the congestion of the prostate gland, so that at the time of the second stage of the operation it is much smaller than the digital examination at the time of the first operation would lead us to believe. This shrinkage of the organ, while serving to add to the difficulties of enucleation, minimizes postoperative bleeding, so that packing to control hemorrhage is less often necessary with the two-stage operation. The success of prostatectomy, let me repeat, is chiefly dependent upon the preliminary treatment; of secondary importance are the technical details with which the enucleation of the prostate is accomplished.

SURGICAL RENAL TUBERCULOSIS: THE PROGNOSIS.[1]

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Several factors affecting the prognosis in cases of surgical renal tuberculosis have not as yet been definitely determined. Probably the most important of these are: Age, sex, coincident tuberculosis in other tissues, duration of symptoms, degree of involvement of the bladder and kidney and bilateral renal disease.

[1] Presented before the American Association of Genito-Urinary Surgeons, June, 1919, Atlantic City.

According to the surgical records of the Mayo Clinic 532 persons were operated on for renal tuberculosis from January 1, 1894, to January 1, 1918. During this period about 85,000 patients were operated on; thus the incidence of surgical renal tuberculosis may be estimated as 0.6 per cent. A previous review[2] has been made of the postoperative records of a portion of these cases, but the present data have been derived from more complete records and a larger number of cases.

The total number of patients (532) was employed in the estimation of many of the general statistics. Among this number were 16 patients who were known to have bilateral renal tuberculosis and were therefore not considered in the survey of postoperative results. Statistics bearing on postoperative results were based on the postoperative records of patients heard from either by correspondence or by personal examination. This number included 435 patients (84.3 per cent.) of those operated on. It will be noted that only the postoperative records of patients operated on prior to January 1, 1918 were studied. In considering the influence of the different complications it was found that more detailed data were available in 346 cases in which operations were performed from January 1, 1912, to January 1, 1918 inclusive.

TABLE I.—AGE.

Patients operated on 532			
2 patients	0 to 10 years	0.4	per cent.
37 "	11 to 20 "	6.9	"
197 "	21 to 30 "	37.0	"
168 "	31 to 40 "	32.0	"
89 "	41 to 50 "	16.7	"
36 "	51 to 60 "	6.7	"
3 "	61 to 70 "	0.6	"

Patients with post-operative data, 435.			Reported dead.
32 patients	11 to 20 years	9 (28.1	per cent.)
161 "	21 to 30 "	41 (26.2	"
137 "	31 to 40 "	26 (18.9	"
75 "	41 to 50 "	20 (26.6	"
27 "	51 to 60 "	7 (25.9	"
3 "	61 to 70 "	1 (33.3	"

The greatest incidence of surgical renal tuberculosis (69 per cent. of the total) occurred between the ages of twenty and forty. The largest number of cases (37 per cent.) is in the third decade. The condition is rarely found in the first and seventh decade. When tuberculous infection of the kidney does occur in children, it is usually in conjunction with tuberculosis disseminated in other tissues so that operation is inadvisable. Nephrectomy in children should not be done with the first onset of symptoms; it is advisable only

[2] Braasch, W. F.: Clinical observations from 203 patients operated on for renal tuberculosis, Jour. Am. Med. Assn., February, 1912, lviii, 397–401.

when it is evident that the active tuberculous infection is localized to the kidney.

The influence of age on the ultimate prognosis is of comparatively little significance and the general mortality average remains fairly constant in the various decades. The late mortality during the third decade is somewhat lower than that during the other decades, but the difference is not great enough to warrant any definite prognostic distinction. In the first and last decades too few cases are involved to give the mortality percentage any accurate value.

TABLE II.—SEX.

Patients	532	
Males	338	(63.5 per cent.)
Females	194	(36.5 "
Patients with postoperative data	435	
Deaths	105	
Males	75	(27.5 "
Females	30	(18.4 "

The greater number of male patients is in keeping with the preponderance of male patients in cases of other chronic infections of the kidney. The relative mortality is somewhat higher in the male. The relative duration of preoperative symptoms is practically the same in both sexes.

TABLE III.—COINCIDENT LESIONS.

Patients with renal tuberculosis operated on from 1912–1918	346	
" with coincident lesions	244	(71.0 per cent.)
" with complete postoperative data	201	
" who died	33	(16.4 "
" with one lesion	89	
" with one lesion who died	14	(15.7 "
" with two lesions	56	
" with two lesions who died	9	(17.8 "
" with three lesions	39	
" with three lesions who died	5	(12.8 "
" with more than three lesions	17	
" with more than three lesions who died	5	(29.4 "

Evidence of tuberculosis in other parts of the body, either healed or active, was found in 244 of the 346 patients (71 per cent.) operated on since 1912. In the examination of a patient with suspected renal tuberculosis a thorough search for such complications is necessary. In fact, it is questionable whether renal tuberculosis ever occurs without coincident tuberculosis in some other tissue, and which may not be apparent on casual examination. That such complications exert but little influence on the ultimate prognosis is evidenced by the fact that the mortality percentage in our cases was even lower when coincident tuberculosis was noted than that of the general average. The occurrence of coincident tuberculosis, particularly when healed or dormant, does not necessarily render the prog-

nosis less favorable; in fact, it may be regarded as an evidence of good resistance power on the part of the patient. In reviewing the postoperative results of the patients with complications, it is of interest to note that when multiple lesions occurred the percentage of recovery was relatively as great as when only one lesion was noted. The only exception occurred when multiple, active complications existed as a part of a generalized tuberculosis. The individual influence of the various coincident tuberculous lesions will be considered separately.

TABLE IV.—COINCIDENT PULMONARY TUBERCULOSIS.

Patients operated on for renal tuberculosis 1912–1918	346	
" having complete postoperative information	298	
" who died	44	(14.7 per cent.)
" having complete *x*-ray and clinical examination of chest	300	
" having definite evidence of pulmonary involvement	81	(27.0 "
" having definite active tuberculosis	16	(5.3 "
" having definite active tuberculosis and complete postoperative information	13	
" who died (none in hospital)	6	(46.3 "
" having doubtful active tuberculosis	17	
" having doubtful active tuberculosis and complete postoperative information	16	
" who died	3	(18.7 "
" having definite healed tuberculosis	26	
" having definite healed tuberculosis and complete postoperative information	21	
" who died	2	(9.5 "
" having indefinite clinical or indefinite evidence of previous pulmonary involvement	22	
" having complete postoperative information	19	
" who died	1	(5.2 "

Pulmonary tuberculosis is one of the most common complications occurring with renal tuberculosis. Fortunately, it is usually found in a chronic or healed form. Renal tuberculosis is not a common complication of active pulmonary tuberculosis. It occurred as a coincident infection in less than 5 per cent. of our patients. As a part of a general or a miliary tuberculosis the coincident infection probably occurs more frequently. Pulmonary tuberculosis as a secondary complication of renal tuberculosis is of relatively infrequent occurrence, although it is a factor in the late mortality after nephrectomy.

Complete roentgen-ray and clinical examinations were made of the chest in 300 patients. Evidence of pulmonary tuberculosis was found in 84 (28 per cent.). The cases were divided into four groups: (1) Definite active tuberculosis; (2) doubtful active tuberculosis; (3) definite healed tuberculosis, and (4) doubtful clinical or roentgen-ray evidence of previous involvement. A number of patients in whom the physical and roentgen-ray data were indefinite were not included.

In Group 1 were 16 patients (4.6 per cent.) of the total number operated on. Fourteen were males and 2 were females. The mortality of this group, as might be expected, was very high; 6 (37.5 per cent.) of the patients died. However, since almost two-thirds of the patients recovered it is evident that active pulmonary tuberculosis does not necessarily exclude operation in cases of renal tuberlosis, but, on the contrary, offers a fair chance for recovery. In the majority of these cases the active pulmonary lesion was confined to comparatively limited areas, diffuse miliary involvement being regarded as excluding operation. In several cases, although the lesions were quite extensive and even bilateral, the general condition of the patients warranted operation. In several cases of well-advanced pulmonary tuberculosis the advisability of operation was doubtful, but it was rightfully argued that an operation offered the only chance of recovery. The most important factor in determining the advisability of operation was the patient's general condition. None of the patients died in the hospital or immediately following operation, showing that the anesthetic (ether in every case), even in the presence of active pulmonary tuberculosis, had no immediate harmful effect.

Group 2 probably includes a small number of patients with limited active lesions. The mortality was approximately average. In Groups 3 and 4 the mortality was unusually low. From this it may be argued that patients with healed pulmonary tuberculosis have developed high resisting powers against the tuberculous infection, and that complicating renal tuberculosis is an evidence that the resistance of patients is only temporarily lowered at the time of the renal infection.

TABLE V.—GENITALIA.

Male patients operated on (1912–1918)	234
Lesions in genitalia	171 (73.0 per cent.)
Complete postoperative data	141
Reported dead	26 (18.4 "
Epididymectomy prior to operation	26
Epididymectomy after operation	24
Patients who died following epididymectomy after operation	3 (12.5 "

Coincident tuberculosis in the genitalia rarely occurs in the female; it was noted as definite in 171 (73 per cent.) of the group of 234 male patients. Twenty-six of these patients (18.4 per cent.) died, 13 during the first year. The late mortality is therefore not greatly influenced by this complication. The high percentage of recoveries among the patients in this group who had clinical evidence of tuberculosis in the prostate and seminal vesicles should contra-indicate surgical treatment of these organs. It is evident that spontaneous healing must occur in the majority of instances. On subsequent examinations the prostate and vesicles are usually diminished in size, and either hard and fibrous or apparently practically normal.

Acute suppuration in the prostate and seminal vesicles is unusual. Surgical treatment of the tuberculous prostate is indicated only in certain cases of protracted vesical irritation or in the presence of suppuration.

Tuberculosis in the epididymis and testicle should be treated surgically because of the frequency of suppuration and because the process does not usually become dormant and disappear. Furthermore, a tuberculous epididymis must always be regarded as a possible focus of general infection. Epididymectomy was done in 50 patients in the series, 26 prior to nephrectomy and 24 following nephrectomy. Three (12.5 per cent.) of the last group are reported dead.

TABLE VI.—BONES AND JOINTS.

Patients with lesions	21 (6.0 per cent.)
Patients with complete postoperative data	19
Patients with lesions described as active	10 (57.8 "
Patients reported dead	1 (5.2 "
Patients with spondylitis	17 (5.7 "
Patients with active spondylitis	3
Patients reported dead (1 active spondylitis)	2 (11.7 "

Tuberculosis, either healed or active, involving the bones and joints, is not unusual with renal tuberculosis. A review of our records shows 21 (6 per cent.) such cases. Of this number 10 were described as active. Four (13.3 per cent.) of the patients are reported dead. Coincident lesions in the bones, even though active, have little or no bearing on the prognosis, provided it is not a part of general acute tuberculosis.

To the group of complications involving the bones should be added the cases of spondylitis. Fourteen patients were suffering with chronic and three with active spondylitis. Two of the former and one of the latter are reported dead, evidence that chronic spondylitis does not greatly affect the ultimate result. Active spondylitis, particularly in the presence of other tuberculous lesions, will necessarily make the prognosis much more serious, but it does not contraindicate operation. One of the patients with an active process operated on six years ago is living, in a fair degree of health. In a number of such patients observed the condition was regarded as inoperable either because of their general health or the presence of other active complications.

Adenitis.

In but 19 (6.4 per cent.) patients was there any well-marked evidence of tuberculous adenitis. In the majority of these only a few glands were involved, and in none sufficiently to require surgical intervention. Two of the nineteen patients (10 per cent.) are reported dead, indicating that this complication has no bearing on

the prognosis other than to show the high resistance on the part of the patient.

TABLE VII.—HEMOGLOBIN.

Patients having less than 80 per cent.	73
Patients reported dead	7 (9 per cent.)
Average duration of bladder symptoms (2 cases without)	2 yrs. 9 mos.
Patients with 50 per cent. or below (one died)	8

Anemia secondary to renal tuberculosis is frequently noted. Its incidence in our series was 25 per cent. As a rule the degree of anemia is not marked. The reduction in hemoglobin is seldom caused by the loss of blood from hematuria. It is not in proportion to the duration of symptoms of the bladder, since a number of patients with low hemoglobin had symptoms of only a few months' duration. The average duration was two years and seven months, which is about the average of all cases. The greatest reduction of hemoglobin is noted with extensive renal suppuration when absorption of toxins was evidently the cause. The degree of hemoglobin gives no index to prognosis; 8 patients had 50 per cent. hemoglobin, or below, of whom 1 died. Seven patients in the series (9 per cent.) are reported dead.

TABLE VIII.—BLADDER INVOLVEMENT.

	Patients.	Dead.	Per cent.	
Degree 1	55	8	14.5	11
Degree 2	92	9	9.7	
Degree 3	71	16	22.5	20
Degree 4	43	7	16.2	

The pathological condition in the bladder as noted on cystoscopic examination in this series is estimated on a scale of 1 to 4; 1 slight involvement; 2 moderate; 3 marked, and 4 extreme. It was found that the patients were about equally divided between moderate (1 and 2) and marked (3 and 4), the largest single group being 3. The average duration of preoperative symptoms when the degree of inflammation was scaled 3 and 4 was two and one-half years, and when it was scaled 1 and 2 it was only one and one-half years. When the preoperative degree of bladder inflammation was slight or moderate (1 and 2) it was found that immediate postoperative improvement in bladder symptoms occurred in 20 per cent., whereas with bladder inflammation graded 3 and 4 immediate improvement was noted in only 10 per cent. The late mortality in cases of moderate bladder involvement (1 and 2) was practically 11 per cent., whereas with advanced involvement (3 and 4) it was 20 per cent., or twice as great. Although the renal disease usually has existed longer in cases of marked bladder involvement, the difference in involvement is evidently more dependent on the virulence of the infection than on the duration of symptoms.

TABLE IX.—DEGREE OF PATHOLOGY.

Patients with complete postoperative data (1912–1918)	298
Patients dead	44 (14.7 per cent.)
Patients with limited lesion	37
Patients dead	2 (4.5 "
Patients with advanced lesion	159
Patients dead	25 (15.7 "
Patients with large pyonephrosis	58
Patients dead	12 (20.6 "
Patients with occluded tuberculosis	44
Patients dead	5 (11.3 "

The conditions of the kidneys removed were divided into four groups: (1) Slight lesions; (2) advanced lesions; (3) complete destruction, described as advanced pyonephrosis; and (4) occluded (caseated) tuberculosis. The lesions in the first group were slight, consisting of limited single areas or multiple early lesions. The mortality in this group (4.5 per cent.) was the lowest and seems to refute the necessity of the patient's development of immunity before the kidney is removed. In by far the largest number of patients the pathological condition of the kidneys was described as advanced (Group 2). Multiple areas involving from one to two-thirds of the kidney substances were usually found. In Group 3 the process has generally existed for so long a time that extensive suppuration has occurred. The mortality is greatest and is probably explained by absorption of toxins from the extensive abscesses, with consequent damage to the other organs. Nevertheless, the most gratifying results are frequently obtained among patients in this group who before their operation are often in extremely poor general condition and afterward become quite normal. Group 4 is in reality a group by itself. It is composed of patients in whom Nature has occluded the ureter, performing a so-called autonephrectomy, and the tuberculous process is supposed to have run its course. In only a few such cases was there any evidence of active tuberculosis in the kidneys; in the majority, the original kidney tissue had undergone caseation. The low mortality is evidenced by the patient's high resisting powers.

TABLE X.—DURATION OF PREOPERATIVE SYMPTOMS.

	Cases.	No change or slight improved.	Markedly improved or practically well.	Dead.
1 to 3 months	30	4 (13.3 per cent.)	18 (60.0 per cent.)	8 (26.6 per cent.)
4 to 12 months	162	33 (20.3 "	87 (53.7 "	42 (25.9 "
1 to 5 years	155	40 (25.8 "	71 (45.8 "	44 (28.3 "
5 years	57	23 (40.3 "	27 (47.3 "	7 (12.2 "
Indefinite	31	4 (12.9 "	23 (74.1 "	4 (12.9 "
Total	435	104 (23.9 "	226 (51.7 "	105 (24.1 "

The influence of the duration of preoperative symptoms on the prognosis might be considered from three phases: (1) Its relation to the severity of the bladder infection; (2) the time elapsing before postoperative improvement, and (3) the postoperative mortality.

Although the severity of the bladder infection is largely dependent on the length of the preoperative symptoms there are other influential factors. It is not uncommon to observe marked inflammation and ulceration with symptoms of only a few weeks' duration. On the other hand a fairly normal bladder is occasionally found when the disease has evidently existed many months. Further, with occluded renal tuberculosis when the initial symptoms had occurred and ceased several years before, the cause of the bladder infection having been removed by autonephrectomy, the bladder usually became fairly normal.

In the majority of cases the duration of vesical symptoms persisting after operation diminished in direct proportion to the length of preoperative symptoms. Of the patients with preoperative symptoms of less than three or four months' duration improvement was noted immediately in 48 per cent. When the symptoms existed a year or more prior to operation immediate improvement was noted in only 15 per cent.

A review of the mortality records shows that there is surprisingly little difference in the mortality with regard to the length of preoperative symptoms of less than five years. It has been claimed that the mortality of patients with short duration of symptoms is considerably higher than that of patients of long duration, and that a relative degree of immunity is established among the latter. This, however, was not borne out in our cases, since the group of patients with symptoms of less than three months had practically the same mortality as the group in which the symptoms were of much longer duration. It is of interest that the mortality in the group of patients having symptoms more than five years is considerably less than the average. This is explained by the fact that many of these patients had either an occluded renal tuberculosis or a high degree of immunity. This group also included five patients who had no evidence of disease other than albuminuria and slight pyuria, and in whom the discovery of renal tuberculosis was largely accidental.

TABLE XI.—BILATERAL RENAL TUBERCULOSIS.

Patients with definite bilateral involvement	16
Patients reported dead (none alive longer than one and one-half years)	13
Patients living (less than two years after operation)	3

It has been claimed that in cases of bilateral renal tuberculosis if the more diseased kidney is removed the patient will often improve, and in certain instances recover. It has also been claimed that infection in the remaining kidney may be reduced or overcome by compensatory hypertrophy; this has not, however, been substantiated by the end-results in our series of bilateral cases. Thirteen of the 16 patients with proved bilateral renal tuberculosis are reported dead; 3 are living. None of the 13 patients lived more than

one and one-half years after operation, and all but 3 died in less than six months. The 3 living were operated on two years before their last report. One of these became steadily worse and recently had complicating perineal fistulas. The general health of the other two has temporarily improved. Both patients had a large, active tuberculous pyonephrosis on one side, which was removed, and a fair degree of function in the other kidney. Such patients improve because the toxemia of acute infection is removed, and not because of improvement in the other kidney. When an occluded caseated kidney was removed, little or no benefit followed. Unless one kidney is largely destroyed and the other is in fair condition, operation should not be considered; and then only when infection, pain, or possibly hemorrhage renders it imperative. Many cases of bilateral renal tuberculosis in which cure by operation was reported in the literature were probably not bilateral. Doubtless pus or tuberculosis bacilli picked up by the ureteral catheter from an infected lower ureter while the kidney itself was normal could best explain such results.

TABLE XII.—MORTALITY.

Operations for unilateral renal tuberculosis	516	
Operative mortality	7	(1.3 per cent.)
Patients with complete postoperative data	435	
Deaths	105	(24.1 "
One year or less after operation	58	(55.2 "
Two years after operation	8	
Three years after operation	6	
Four years after operation	2	
Five years after operation	7	
Six years after operation	5	
Seven years after operation	3	
Eight years after operation	1	
Nine years after operation	1	
Ten years and over after operation	1	
Date of deaths not given	13	

The operative mortality (1.3 per cent.) is a comparatively negligible factor. The total mortality (excluding bilateral renal tuberculosis) is 24 per cent., which includes every death from any cause following operation, some occurring as long as ten or more years afterward.

Fifty-eight patients (55 per cent.) died within one year after operation. The relatively high mortality during the first year after operation has been previously noted by several observers. It would seem logical to regard the early death as an evidence of the virulence of the infection rather than as a result of the operation. It may be inferred that the probability of death from tuberculosis decreases inversely with the length of time after operation. Owing to the inability to get accurate data as to the cause of postoperative death, no attempt was made to investigate this factor.

Many patients died from diseases other than tuberculosis and from accidents, so that the late mortality from tuberculosis is really

much less than our figures indicate. Furthermore, a considerable proportion of the total number of deaths reported occurred more than five years after operation. It would be conservative and more accurate, therefore, to regard the actual late mortality as not more than 20 per cent.

One hundred and four (23 per cent.) of the living patients stated that they had not entirely recovered from their bladder symptoms. From many of these answers to inquiries were received in less than two years after operation, and it is safe to assume that at least 5 per cent. would eventually report recovery from their symptoms. Moreover, 64 patients reported a gain in weight and general condition, so that except for the bladder symptoms they were in a fairly good state of health.

It may be assumed, therefore, that approximately 80 per cent. of the patients will recover following operation for renal tuberculosis and that a complete cure, including cessation of urinary symptoms, may be expected in fully 60 per cent.

Conclusions.

1. Renal tuberculosis occurs most frequently between the ages of twenty and forty years (70 per cent.).
2. It occurs in the male almost twice as often as in the female.
3. The postoperative mortality in the male patient is somewhat higher than in the female.
4. The condition is usually not surgical in children; it occurs more often as a part of a general tuberculosis.
5. Evidence of tuberculosis in other tissues of the body may be found in fully 71 per cent. of the patients, if not in all.
6. The postoperative mortality among patients with coincident lesions is not higher than that of the general average.
7. Multiple lesions, unless they are a part of an acute general infection, do not necessarily render the prognosis more unfavorable.
8. Evidence of healed pulmonary tuberculosis is present in fully one-third of the patients.
9. The percentage of recovery among patients with healed pulmonary tuberculosis is above the average and may be considered indicative of increased powers of resistance.
10. Coincident active pulmonary tuberculosis was found in approximately 5 per cent. of the patients, of whom more than 60 per cent. recovered following nephrectomy.
11. Involvement of genitalia is present in at least 73 per cent. of male patients and does not seem to affect the ultimate recovery.
12. Frequency of spontaneous healing of lesions in the prostate and seminal vesicles contra-indicates their removal by subsequent operation.

13. Evidence of tuberculosis involving the bones and joints was noted in 6 per cent. of the cases; one-half of the lesions were active. The late mortality was 5 per cent., from which it may be inferred that the presence of such complications may be an index of increased resistance.

14. Spondylitis, usually healed, was present in 5.7 per cent., with a mortality of 12 per cent.

15. Chronic spondylitis does not influence the prognosis. Active spondylitis, although it does not contra-indicate nephrectomy, will not offer a favorable prognosis.

16. Tuberculous adenitis was present in 19 patients (6.4 per cent.) and the low mortality (10 per cent.) is suggestive of a heightened resistance.

17. Reduction in hemoglobin does not necessarily affect the prognosis.

18. The mortality among patients with marked bladder involvement is twice as great as with slight involvement. The degree of involvement is dependent not so much on the duration of symptoms as on the virulence of the infection.

19. The mortality percentage is markedly influenced by the degree of pathological involvement of the kidney, increasing in proportion to the extent of the lesion. Early lesions have the lowest mortality and pyonephrosis the highest.

20. Occluded renal tuberculosis is indicative of relative immunity and a low mortality.

21. The duration of preoperative symptoms does not materially affect the late mortality.

22. Recovery from bladder symptoms is more apt to occur, and earlier, when the preoperative symptoms are short than when they are long.

23. Recovery or permanent improvement of the remaining kidney will not follow after one kidney has been removed in cases of bilateral renal tuberculosis.

24. Operation in cases of bilateral renal tuberculosis is advisable only when there are acute unilateral complications, and then with no hope of eventual recovery.

25. Late mortality is much the highest during the first year; it decreases with the length of time elapsing after operation.

26. The operative mortality is a negligible factor; the late mortality (five years or less after operation) is approximately 20 per cent.; failure to effect complete cure is approximately 20 per cent.; this leaves a prognosis of recovery in 80 per cent. and of a complete cure to be expected in fully 60 per cent. of patients.

DIAGNOSTIC SIGNIFICANCE OF THE FIRST SOUNDS OF THE HEART.

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Circular 21, S. G. O.,[1] issued especially to the cardiovascular examiners is a definite statement of the most advanced standpoint in the diagnosis of heart conditions, and as such deserves to be called to the attention of all clinicians.

One of the most striking features of Circular 21 is the absolute disregard of the systolic murmur, the interpretation of which is usually considered the ultimate test of our diagnostic ability. Lewis[2] had previously called attention to the lack of agreement among physicians as to the meaning of the various types of apical systolic murmurs. But neither Lewis, nor Janeway in Circular 21, offered a substitute standard for cardiac examinations.

Such a standard, I think, may be found by comparing the first sound over the right and left ventricles. Dana's[3] recent confirmation of this idea leads me to believe that a statement as to the possibilities of this method would not be without interest.

The cause of the first sound of the heart seems to be an accepted physiological fact. At least the description varies little in the text-books, and all agree in stating two factors, muscle contraction and auriculoventricular valve tension. As one studies the effects of mitral valve lesion on the first sound, one is led to doubt the usual explanation, at least, as applied to muscle contraction. If, however, one can consider the first sound as due to tension in muscle as well as in valve the changes in the first sound as a result of valve and muscle disease can be easily understood.

The theory of Martius, supported by Howell, that the first sound begins during the time of total closure of the ventricle, that is, when there is no movement of the blood within the chamber, seems to substantiate the idea that almost the entire first sound is a result of tension of both valve and muscle. It is true that the first sound lasts longer than the time of total closure, but it is also true that when there can be no total closure, that is, with mitral regurgitation, the first sound, making all allowance for the peculiarities of conduction, is absent. The laws of conduction of sound within the chest are but slightly understood, and for this reason the interpretation of sound heard must always be based upon changes in conduction as well as in character.

[1] Circular 21, Surgeon-General's Office, July, 1917.
[2] Medical Research Committee, Special Report No. 8, London, 1917.
[3] Heart Muscle Equation, Am. Jour. Med. Sc., June, 1919.

The evidence obtained by percussion in the examination of the heart is valuable in many instances, but in the very case where most needed a rigid thorax, an emphysema or some one of the other sources of error makes the result of percussion uncertain. When one has seen a clear-cut stereoscopic radiograph of the heart and mediastinum one is not inclined to rely very much upon the percussion outline.

So with systolic murmurs under suspicion as diagnostic criteria, and percussion outline unreliable, any procedure which will give definite information is to be utilized to the utmost. And such a source of information is to be found in the study of the first sounds of the heart.

Exactly the same series of events occur synchronously in the right and left heart, with the result that the normal heart sounds thus produced are fused into a single first sound; but just as we have been taught to differentiate systolic murmur by the point of maximum intensity and the direction of transmission, so we can learn to tell the first sound as created in the right heart from that in the left by studying these sounds at the point of optimum clearness. The sounds then can be compared by auscultation, first, over the right ventricle and then over the left. In the fourth or fifth interspace, just to the left of the sternum, the right first sound is heard most clearly, but considerable liberty of selection is allowed in order to find the place where there is the least possible interference from conduction. The first sound originating in the left ventricle is best heard just above and within the apex-beat, the classic area of mitral stenosis murmurs. How much depends upon the proper selection of these areas to avoid confusion can best be realized when one remembers the definite localization of the very loud presystolic murmur and snappy first sound of mitral stenosis.

In a normal heart the first sound right and left are practically the same in length and quality of tone, but the right not quite so loud.

The first sound over the right ventricle is almost always normal or standard, because disease of the tricuspid valve is rare, and such hypertrophy as occurs here is in total amount so slight that changes in sound due to this are beyond our interpretation.

Considering, then, the right first sound as the individual standard; comparing this with the left first sound as heard at the apex, we find that the left first sound may be increased, diminished, absent or show complete changes in character.

The increased first sound left is perhaps best typified by the booming first sound of aortic insufficiency. This seems to be due to increased muscle tension and varies directly with the amount of hypertrophy of the left ventricle and with the condition of the heart muscle. The first sound in infectious aortic insufficiency is louder and longer than in degenerative aortitis, in which there are usually

heart muscle changes as well. Hypertrophy of the left ventricle from any cause produces similar changes in tone quality of the first sound left, but when the hypertrophy is bilateral the tone quality of the right first sound is also affected, and then differentiation is more difficult.

According to Martius the first sound left must be absent in mitral insufficiency because this lesion makes it impossible for the left ventricle to have a "time of total closure."

In a very large proportion of the cases of pure mitral insufficiency we do not hear a first sound left, and it is perfectly safe to make a diagnosis of organic regurgitation, upon this combination of no first sound at the apex and a loud systolic murmur, with normal first sound right. Likewise, it is impossible to substantiate a diagnosis of mitral insufficiency when there is systolic murmur and a normal first sound left. Difficulty arises when a changed first sound left and murmur is heard, and in such instances a very careful examination is necessary to determine whether the first sound heard at the apex is conducted from the right side or whether, in truth, the first sound originates within the left ventricle. If the first sound has the same quality and tone as a normal first sound left, but is merely shorter in duration and followed by a murmur, the exercise test will many times cause the sound to disappear and be replaced, in its entirety, by a systolic murmur. Under these circumstances we have no hesitancy in diagnosing myocardial degeneration with relative mitral insufficiency. Even without the systolic murmur, shortening of the first sound left, with changes which seem to be due to lack of muscle tone, can frequently be changed by exercise into a definite systolic murmur without first sound; and here, again, we are justified in making a diagnosis of myocarditis with relative mitral insufficiency.

When the first sound as heard at the apex is shorter than the normal first sound on the right side, and of slightly different tone quality, the change not due to conduction and persisting through the exercise test, one must either dismiss entirely the diagnosis of mitral insufficiency or add thereto the diagnosis of mitral stenosis. The correct diagnosis can be made by a careful study of diastole in various postures and with different amounts of exercise, keeping well in mind the typical exercise response of mitral stenosis, which consist in suddenly developing dyspnea and peripheral cyanosis. Even when no murmurs can be heard in diastole this first sound may be an approach toward the snappy first sound of mitral stenosis, and must be considered as indicating possibly an early phase of mitral disease of the progressive type, which will ultimately develop a predominating stenosis.

The buttonhole mitral stenosis gives the most typical snappy first sound, which may be likened to the sound of a single stroke on the tambourine. For the purpose of comparison it may be said that

the valve element dominates this sound exactly as the muscle element dominates in booming first sound. Mitral stenosis can scarcely be diagnosed without the snappy first sound, but this, in addition to practically any form of diastolic murmur, save that of aortic insufficiency, means mitral stenosis.

In those cases of mitral stenosis presenting 3–4 rhythm, it must be remembered that the second of the sounds is the true first sound and is the one which has the characteristic tambourine quality.

When one has learned the difference in tone quality of the right and left first sound in a typical case of buttonhole mitral stenosis it is then much easier to pick out the changes described in the preceding paragraphs. It must be remembered that in double mitral lesions we cannot determine by auscultation which defect dominates in disturbing the physiology of the circulation. This important differentiation depends entirely on the size of the left ventricle, as shown by the position of the apex-beat and the percussion outline.

If we rely upon this classic combination of presystolic thrill, presystolic roll and snappy first sound, we will be able to diagnose only 30 to 40 per cent. of the cases of mitral stenosis. Any change in first sound left should direct our attention to a more careful survey of diastole, and we will then be able to recognize the early and atypical cases of mitral stenosis.

The first sound in Graves's disease is shortened both right and left and has a rather peculiar stroke, which allows one to differentiate it clearly from an equally rapid systole, due to other conditions. Usually in these rapid pulse cases the first sound right and left are similar, but in certain cases of neuro-circulatory-asthenia the right first sound remains normal while the left first sound takes on the quality of thyroid heart. It is interesting to note, however, that in those neuro-circulatory-asthenia cases which respond unfavorably to exercise from very slight exertion the right first sound also becomes quicker and shorter and approximates the left first sound.

In approaching death from infectious disease and also in so-called surgical shock cases there is a gradually increasing loss of tone in the first sound, both right and left, until twenty-four to thirty-six hours before death, we have the tick-tack heart in which the first and second sounds are alike, and from six to twelve hours before death one sound is lost, and upon the most careful auscultation only the single sound can be heard.

Incidentally, I may remark that after the stage of the tick-tack sound is reached I have never seen any form of stimulation bring about a reaction on the part of the heart muscle, although up to this stage, stimulation, preferably with the caffein group, frequently brings about marked improvement.

Reduplication of the first sound is by no means infrequent, but as long as the reduplication occurs without disturbing the 2–4 rhythm of the heart no importance is to be attached to this. On

the contrary, when the extra sound changes the rhythm from 2–4 to 3–4 gallop rhythm it is always of the utmost significance. When we study this rhythm by comparison of the first sound right and first sound left, we find it almost always limited to the left ventricle, occasionally to the right, but exceptionally it may occur over both.

The synonym rhythmus brightique is given to this condition because it most frequently occurs in the left ventricle hypertrophied as a result of arteriosclerotic kidney, but it can occur in any form of hypertrophied heart muscle. The occurrence of the 3–4 rhythm localized over the right ventricle is not uncommon in kyphosis and other extreme deformities of the chest. This 3–4 rhythm always means degenerative hypertrophic heart muscle, which is on the verge of "failure" in Mackenzie's interpretation of this word.

Furthermore, demonstration of the 3–4 rhythm is a positive indication for the administration of digitalis which will usually restore the normal rhythm. If not treated with digitalis the case very soon progresses to the usual manifestations of conclusive decompensation. Since a very much larger percentage of cardio-vascular-renal cases finally break under heart symptoms than is generally believed, eliciting this 3–4 rhythm as an early sign of approaching heart muscle weakness, is of great value.

Behavior of the first sound in the various forms of cardiac irregularity presents many interesting features. For instance, in mitral insufficiency of the type described above the long systolic murmur and no first sound, with ectopic beats, the first sound is heard over the apex with the premature contraction, and usually seems louder, the earlier and more incomplete the ectopic beat. This also holds true in cases of tricuspid insufficiency where the same condition can be demonstrated over the right ventricle.

In mitral stenosis with fibrillation the snappy first sound is heard only with those systoles which present a normal pulse wave, and inasmuch as fibrillation of the auricle does away with practically all diastolic murmurs a diagnosis of mitral stenosis again depends upon comparison of the first sound right and left.

I am quite aware that I have presented nothing new, and nothing that is not to be found, better described, in the text-books on physical diagnosis, but the fact remains that the teaching of physical diagnosis has always laid undue importance upon systolic murmurs in the study of the heart, and sounds have been neglected. Each clinician must learn for himself to interpret the phenomena of the heart, and in so doing he places more or less importance upon the sounds; but, unfortunately, he does not formulate this knowledge in such a way that it is available for demonstration, and what I have offered here is merely a suggestion to substitute for an illy defined memory picture of the first sound of the heart the normal standard of the right first sound.

REPORT OF DIABETIC SERVICE AT U. S. ARMY GENERAL HOSPITAL NO. 9, LAKEWOOD, NEW JERSEY.

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and
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The special diabetic service which was in operation in this hospital from the end of July, 1918, to the end of May, 1919, was the only one of the kind in the American army and was intended to receive all diabetic cases developing in the more easterly districts of this country or returning from overseas. Owing to imperfect notification and other obstacles, by no means all such cases were actually assembled here, so that the statistical value of this report is limited. Of the total number of 40 cases received, 3 proved to be so-called "renal glycosuria" and have been reported elsewhere.[1] Three others (Nos. 8, 16 and 37 below) have also been described separately[2 3 4] because of certain special features. A summary of the observations concerning the entire 37 diabetic cases may be desirable as a record of military experience and for its instructiveness in some details.

Organization of Service. An old hotel had been taken over for the hospital and it was necessary to improvise everything for the diabetic as for other services. The barber shop was transformed into a chemical laboratory and a bedroom and adjoining bath on the ward were made into a diet kitchen. With a suitable chemical staff and equipment, experienced nurses and the cordial support of the commandant and other authorities it was proved that accurate and effective treatment could thus be carried out.

Study of Cases. The study was aided by the military requirement of a series of routine examinations and the coöperation of specialists in the various branches of medicine. The presence or absence of abnormalities was determined not only by general physical examination but also with the assistance of the eye, ear, nose and throat and dental, cardiac (including electrocardiographic), surgical, orthopedic, genito-urinary, radiographic, bacteriological and general laboratory services. The data obtainable have thus been increased in extent and value and the cordial helpfulness and absence of antagonism or intrigue also made this phase of the work a pleasure.

[1] Allen, Wishart and Smith: Three Cases of "Renal Glycosuria." The Archives Int. Med., November 15, 1919.
[2] Mitchell: Amer. Jour. Med. Sc., May, 1919, p. 700, vol. clvii, 5.
[3] Allen and Mitchell: A Case of Hereditary Diabetes. Publication forthcoming.
[4] Allen and Mitchell: A Case of Uncontrollable Diabetes. Publication forthcoming.

Case No.	Rank.	Age.	Race.	Civil occupation.	Family history.	Personal history.				Physical examination.									
						Diseases.	Military service years.	Time elapsed.		Height.	Weight.			Teeth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.	Wassermann.
								From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.		Ordinary.	Admission.	Discharge.						
1	Capt.	40	Amer.	Physician	Father and one brother diabetic Family obese	Mumps, measles and chicken-pox as a child	4/12 not overseas	Few months	Immediately	6 ft. 4 in.	280	260	240	Negative	Negative	Negative	Negative	Negative	Neg.
2	Capt.	41	Amer.	Post office employee	Maternal grandfather died of diabetes	Mumps, measles and scarlatina as child	1 7/12 not overseas	Two months	Two weeks	5 ft. 10 in.	170	170	145	Negative	Negative	Negative	Negative	Knee-jerks diminished	Neg.
3	Capt.	55	Amer.	Newspaper reporter	No diabetes or obesity	Mumps in childhood	1 2/12 overseas. Shock and head injuries	Unknown	Unknown period of years	5 ft. 10 in.	210	180	145	False	Negative	Palpable posterior cervicals	Liver palpable 2 cm. below costal margin	Knee-jerks increased	Blood ++ sp. fl. ++
4	2d Lt.	37	Amer.	Metal miner	Maternal relatives obese	Mumps, measles, whooping-cough and scarlatina as child. Typhoid at 10 yrs. Malaria at 22 yrs.	3 5/12 not overseas	Two months	Immediately	5 ft. 10 in.	145	145	135	Negative	Negative	Palpable posterior cervicals	Arteriosclerosis, early	Negative	Neg.
5	1st Lt.	34	Amer.	Physician	Father died malignancy, 1 bro. of nephritis. No diabetes or obesity	Mumps, measles and chicken-pox in childhood	1 4/12 overseas	Intermittent glycosuria foronemonth no other symptoms	One month	5 ft. 8 in.	200	215	153	Negative	Negative	Negative	Scar of penetrating wound, left chest posterior	Negative	Neg.
6	Capt.	45	Eng.	Physician	No diabetes or obesity	Influenza, Sept. 18	1 3/12 overseas	One month	Three months	5 ft. 5 in.	145	137	126	Pyorrhea and caries	Negative	Negative	Negative	Negative	Neg.
7	Capt.	44	Amer.	Soldier	Familial obesity	Measles and whooping-cough as child. Malaria in 1889; tropical liver 1906; influenza, Oct. '18	22 not overseas	One month	Four months	5 ft. 11 in.	225	180	155	Negative	Negative	Negative	Heart enlarged to left. Liver palpable 5 cm. below costal margin	Knee-jerks absent Romberg positive. Sensation impaired lower extremities	Blood neg. sp. fl. neg.
8	Lieut. Naval	43	Canada	Marine eng.	No diabetes or obesity	Mumps and diphtheria in childhood	1 8/12 torpedoed	10 days	Immediately	5 ft. 9 in.	190	130	120	Negative	Negative	Inguinal adenopathy	Liver palpable 3 cm. above umbilicus. Maximum ascites, bilateral hydrothorax	Knee-jerks absent	Neg.

Case No.	Symptoms. Glycosuria.	Acetonuria.	Plasma sugar %	Plasma CO_2 combining power vol. %	Clinical.	Stay in hospital months.	Maintenance diet. Protein.	Carbohydrate.	Calories.	Faithful to diet.	Other treatment.	Plasma sugar under treatment.	Prognosis and reasons.	Remarks
1	Heavy	Negative	0.356	....	Irritability; polyphagia, polydipsia, polyuria and loss of weight and strength	2	100	125	3000	Yes	None	0.356–0.102	Good. Age and training.	Obese type.
2	Heavy	Heavy	0.400	....	Polyuria; polydipsia; xerostoma	2	70	60	1800	Fair	None	0.400–0.100	Fair. Age in patient's favor, but accidents are liable, as diabetes is not very seriously considered	
3	Faint	Faint	0.250	....	Loquacious; slovenly; grandiose; no diabetic symptoms	3	70	40	2000	Fair	KI, mercury and salvarsan	0.25 –0.09	Bad. Early paresis	Patient states that glycosuria was present over a long period; could not remember exact date of discovery.
4	Moderate	Moderate	0.200	....	Polydipsia; polyuria; polyphagia; failing vision	1	70	50	1800	Yes	None	0.200–0.105	Good. Age and intelligence	
5	Faint	Moderate	0.129	59.5	No symptoms.	3	70	100	2000	Yes	None	0.129–0.106	Good. Mild case; profession	Glucose tolerance (100 gm.) Dec. 16, 1918. Plasma sugar, % / Urine, vol. c.c. / Urine, sugar, % I. 0.090 / 16 / Neg. (fasting) II. 0.250 / 75 / 3.33 III. 0.150 / 110 / 3.40 IV. 0.126 / 148 / 0.32
6	Heavy	Faint	0.18	55.5	Nervousness; irritability; no classical symptoms	3	None	could be	prescribed	No	None	0.15 –0.10	Bad. Lack of intelligence and persistent slight hyperglycemia	Glucose tolerance (50 gm.) Jan. 17, 1919. Plasma, sugar, % / Urine, vol. c.c. / Urine, sugar, % I. 0.136 / ... / (Fasting) II. 0.250 III. 0.273 / 38 / 0.50 IV. 0.250 / 135 / 0.25 V. 0.158 / 175 / Negative
7	Heavy	Faint	0.356	....	Polyuria; polyphagia; polydipsia; loss of weight and strength; dizziness and incoördination	3	80	80	2000	Yes	Physiotherapy	0.356–0.10	Good. Age, type and fidelity	Obese type.
8	Heavy	Heavy	0.450	....	Polyuria; polydipsia; polyphagia; loss of weight and strength; general anasarca; ascites and dyspnea	9	70	10	1500	No	Physiotherapy	0.400–0.12	Poor. Luetic cirrhosis and mental attitude	*Ascitic fluid gave two plus Wassermann Dec. 12, 1919. One week following provocative dose of salvarsan the blood Wassermann was one plus (army nomenclature).

Case No.	Rank.	Age.	Race.	Civil occupation.	Family history.	Personal history.				Physical examination.									
						Diseases.	Military service years.	Time elapsed.		Height.	Weight.			Teeth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.	Wassermann.
								From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.		Ordinary	Admission.	Discharge.						
9	2d Lt.	25	Amer.	Metallurgical engineering	No diabetes or obesity	Mumps, measles, scarlet and chicken-pox as child. Appendicitis, 1917, pus case	1 5/12 overseas	One month	Two months	5 ft. 6 in.	140	130	120	Negative	Negative	Negative	Negative	Negative	Neg.
10	Pvt.	23	Amer.	Clerk	One brother obese, no diabetes	Mumps and measles in childhood	11/12 not overseas	Two months	Immediately	5 ft. 6 in.	130	102	100	Negative	Negative	Cervicals palpable	Depression of old skull fracture	Negative	Neg.
11	Pvt.	21	Amer.	Laborer	No diabetes or obesity	Denies all diseases	8/12 not overseas	Two months	Immediately	5 ft. 9 in.	150	138	130	Negative	Chronic tonsillitis	Negative	Negative	Negative	Neg.
12	Corp.	23	Amer.	Teamster	No diabetes or obesity	Measles as child. Tonsillitis at onset of diabetes	5 3/12 overseas	Two months	One and one-half months	6 ft. 1 in.	188	130	125	Negative	Chronic tonsillitis (tonsillectomy)	General adenopathy	Negative	Knee-jerks diminished	Neg.
13	Cook	28	Amer.	Cook	No diabetes or obesity	Measles as child	11/12 not overseas	At once	Two and one-half months	5 ft. 10 in.	154	119	115	Negative	Negative	Negative	Negative	Rt. knee-jerk absent	Neg.
14	Sgt.	41	Amer.	Civil engineer	Father died following gallbladder operation. No diabetes or obesity	Measles and scarlet fever as child. Furunculosis, 1915; influenza, Oct., 1918	1 not overseas	Three months	Six months	5 ft. 8 in.	175	152	135	Negative	Negative	Negative	Negative	Knee-jerks diminished	Neg.
15	Pvt.	22	Amer.	Cotton mill worker	Father died apoplexy. 6 sisters and brothers died with diabetes	Mumps, measles, chicken-pox and smallpox as child. Rectal fistula in 1917, very chronic	7/12 overseas	Existed prior to military service; discovered accidentally	Three months, army diagnosis.	5 ft. 11 in.	158	104	...	Caries	Chronic tonsillitis	General adenopathy	Entire left lung and right lower dull with crepitant rales. Fluid in right chest	Knee-jerks absent	Neg.
16	Ex-Sgt.	32	Amer.	Clerk	No diabetes or obesity	Measles, mumps and diphtheria as child. Frequent tonsillitis. Chancre, 1908	7 not overseas	One month	Immediately	5 ft. 7 in.	130	100	95	Negative	Chronic tonsillitis	Negative	Negative	Knee-jerks diminished	Neg.
17	Pvt.	19	Amer.	Clerk	No diabetes or obesity	Measles and typhoid as child	11/12 not overseas	Six months	Immediately	5 ft. 8 in.	160	130	122	Negative	Chronic tonsillitis	Cervicals palpable	Negative	Knee-jerks diminished	Neg.
18	Pvt.	30	Dutch	Farmer	3 brothers tuberculous. No diabetes or obesity	Measles as child	5/12 not overseas	One month	Two months	5 ft. 8 in.	150	140	126	Negative	Negative	Negative	Negative	Negative	Neg.
19	Pvt.	21	Amer.	Gunsmith	3 aunts tuberculous. No diabetes or obesity	Denies all diseases	2 not overseas	Five months	Immediately	5 ft. 11 in.	158	135	130	Negative	Negative	Negative	Negative	Negative	Neg.

	Symptoms.					Stay in hospital months.	Maintenance diet.			Faithful to diet.	Other treatment.	Plasma sugar under treatment.	Prognosis and reasons.	Remarks.
	Glycosuria.	Acetonuria.	Plasma sugar %	Plasma CO_2 combining power vol. %	Clinical.		Protein.	Carbohydrate.	Calories.					
9	Moderate	Negative	0.231	71.0	Polyuria; polydipsia; loss of weight and strength	3	75	100	2000	Yes	None	0.231–0.106	Fair. Intelligent, but youthful type	
10	Heavy	Moderate	0.204	....	Polyuria; polydipsia; polyphagia; blurred vision; loss of weight and strength	4	70	25	1200	No	None	0.220–0.106	Poor. Lack of intelligence and poor environment	
11	Heavy	Heavy	0.490	....	Polyuria; polyphagia; insomnia	6	70	25	1200	No	None	0.250–0.067	Poor. Ignorance and lack of will power.	
12	Heavy	Heavy	0.345	....	Tonsillitis; polyuria; polyphagia; polydipsia; pruritus; loss of weight and strength	5	70	80	2000	Fair	Tonsillectomy	0.500–0.064	Doubtful on account of environment	
13	Heavy	Heavy	0.278	....	Lassitude and furunculosis	3	60	10	1200	No	None	0.800–0.075	Bad. Ignorance and weak will	Died (Feb. or March, 1919).
14	Heavy	Heavy	0.378	....	Polyuria; polyphagia; polydipsia; loss of weight and strength	5	70	60	1800	No	None	0.378–0.086	Bad. Weak will and inherent severity of case	
15	Heavy	Heavy	0.800	23.0	Polyuria; polydipsia; polyphagia; weakness; loss of weight; cough; chest pain	5	70	50 to 0	1500–2000	No	Fresh air	0.800–0.125	Bad. Advanced tuberculosis and severe diabetes	Died May 9, 1919.
16	Heavy	Heavy	0.600	76.7	Polyuria; polyphagia; polydipsia; loss of weight and strength	3½	70	10	1200	No	None	0.25 –0.084	Bad. Inherent severity of case and lack of will power	Blood Wassermann positive in 1908, negative 1911, two plus 1915 and negative in 1917. Spinal puncture negative in 1915.
17	Heavy	Heavy	0.470	....	Polyuria; polydipsia; polyphagia; lassitude; dizziness	4½	70	50	1800	Yes	None	0.210–0.09	Good. Intelligent; good environment	Died March 2, 1919.
18	Heavy	Heavy	...	....	Polydipsia; polyuria	4	70	50	1800	Fair	None	0.178–0.077	Bad. Poor environment and ignorance	
19	Heavy	Heavy	0.400	....	Polyuria; polydipsia; loss of weight	4	70	80	2000	No	None	0.500–0.095	Bad. Untrustworthy	

Case No.	Rank.	Age.	Race.	Civil occupation.	Family history.	Personal history.				Physical examination.									
						Diseases.	Military service years.	Time elapsed.		Height.	Weight.			Teeth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.	Wassermann.
								From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.		Ordinary.	Admission.	Discharge.						
20	Corp.	30	Amer.	Cement contractor	No diabetes or obesity	Measles, chickenpox and whooping cough as child	7/12 overseas	Two months	Two months	5 ft. 8 in.	146	127	125	Negative	Chronic tonsillitis	Palpable cervical and inguinals	Negative	Knee-jerks diminished	Neg.
21	Pvt.	20	Amer.	Electrical engineering	Father died nephritis. Maternal uncle diabetic, obese type	Mumps and measles as child. Pneumonia in Dec., '17 and Oct., '18. Otitis media, bilateral, after onset of diabetes	1 overseas	One week	Immediately	5 ft. 10 in.	150	95	...	Negative	Chronic tonsillitis	Negative	Otitis media, bilateral	Knee-jerks diminished	Neg.
22	Corp.	24	Polish	Chain maker	No diabetes or obesity	Tonsillitis at 21	1 1/12 overseas. Gas and shock	One month	Attempted at once; impossible in field hospital	5 ft. 11 in.	152	118	115	Negative	Chronic tonsillitis	Palpable cervicals	Negative	Knee-jerks absent	One plus.
23	Pvt.	22	Negro	Farmer	No diabetes or obesity	Mumps and malaria as child. Respiratory infection preceding discovery of diabetes	7 weeks not overseas	Two months	Immediately	5 ft. 5 in.	125	132	130	Carious, 2 abscessed	Chronic tonsillitis	General adenopathy	Negative	Negative	Neg.
24	Pvt.	28	Negro	Laborer	Father, mother and only sister dead, cause unknown. Only brother tuberculous	Chills and fever every year	7/12 overseas	Existed prior to military duty	Four months	6 ft. 1 in.	160	153	145	Carious	Negative	General adenopathy	Negative	Negative	+ +
25	Pvt.	24	Jew	Printer	Mother died of diabetes. Cousin died of diabetes at 10 yrs.	Denies diseases of childhood. Never enjoyed good health, no stated reason	5/12 overseas	Two weeks	One and one-half months	5 ft. 10 in.	155	115	107	Carious	Chronic tonsillitis	Negative	Negative	Negative	Neg.
26	Pvt.	25	Amer.	Automechanic	Father died of heart condition. Mother is diabetic. Both grandmothers died of either nephritis or diabetes	Mumps, measles and whooping-cough as child	11/12 overseas	No symptoms	Two months	5 ft. 7 in.	120	137	114	Slight caries	Chronic tonsillitis	Negative	Negative	Negative	Neg.

Case No.	Symptoms. Glycosuria.	Acetonuria	Plasma sugar %	Plasma CO_2 combining power vol. %	Clinical.	Stay in hospital months.	Maintenance diet. Protein.	Carbohydrate.	Calories.	Faithful to diet.	Other treatment.	Plasma sugar under treatment.	Prognosis and reasons.	Remarks.
20	Heavy	Moderate	0.240	....	Polyuria; polyphagia, polydipsia; loss of weight and strength	4	80	80	2200	Yes	None	0.240–0.096	Good. Reliable and intelligent	
21	Heavy	Heavy	0.300	27.0	Polyuria; polyphagia; polydipsia; failure to gain weight following influenza	1	....	....	....	Yes	Ear irrigations and local applications	0.300–0.132	Poor. Infections present and severity of case	Died Jan. 16, 1919, of acute streptococcic meningitis secondary to otitis media. On day before death the plasma sugar was 0.195 per cent. and the CO_2 combining power 63.3 vol. per cent.
22	Heavy	Heavy	0.312	57.6	Polyuria; polyphagia; polydipsia; loss of weight and strength	3½	100	100	1900	Yes	None	0.440–0.097	Good. Intelligent and reliable	
23	Heavy	Slight	0.25	....	Polyuria; polyphagia; polydipsia; weakness; pain in back	3	75	75	2000	No	None	0.25 –0.095	Bad. Ignorance and poor environment	Continuous acetonuria due to breaking diet.
24	Heavy	Faint	0.696	....	Polyuria; "trench feet," with loss of distal phalanges of all toes (gangrene?)	3	75	75	2000	No	Mercury and salvarsan	0.696–0.110	Bad. Ignorance and poor environment	
25	Heavy	Heavy	0.313	....	Polyuria; polyphagia; polydipsia; loss of weight and strength	3	70	70	1800	No	None	0.454–0.122	Bad. Ignorance and untrustworthiness	
26	Negative	Negative	0.125	....	No symptoms	4	70	100	1500	Yes	None	0.125–0.106	Poor. Ignorance	An inherently mild case, but with continuous acetonuria.

Case No.	Rank.	Age.	Race.	Civil occupation.	Family history.	Personal history.				Physical examination.									
						Diseases.	Military service years.	Time elapsed.		Height.	Weight.			Teeth.	Tonsils.	Lymph glands.	Viscera.	Nervous system.	Wassermann.
								From first diabetic symptoms to the diagnosis.	From diagnosis to institution of dietotherapy.		Ordinary	Admission.	Discharge.						
27	Pvt.	26	Amer.	Machinist	No diabetes or obesity	Measles and chicken-pox as child	1 7/12 overseas	One month	Two months	5 ft. 6 in.	135	97	98	Negative	Negative	Negative	Pendulous abdomen. Dulness at left apex	Negative	Neg.
28	Pvt.	27	Amer.	Food chemist	No diabetes or obesity	Mumps, measles and chicken-pox as child. Pneumonia at 15 yrs. Jaundice in 1916, 1917 and 1918	11/12 overseas	One week	Immediately	5 ft. 5 in.	126	126	120	2 abscessed	Negative	Palpable posterior cervicals	Slight epigastric tenderness. Spleen palpable	Negative	Neg.
29	Pvt.	27	Amer.	Clerk	No diabetes or obesity	Measles and typhoid as child	7/12 overseas	Ten days	Immediately	6 ft.	150	146	131	Caries	Negative	Negative	Negative	Knee-jerks diminished	Neg.
30	Corp.	36	Amer.	Steam fitter	No diabetes or obesity	Mumps, measles and chicken-pox as child	6 9/12 not overseas	Five months	Immediately	5 ft. 8 in.	210	162	140	Crowns and bridges, no abscesses	Chronic tonsillitis	Negative	Negative	Knee-jerks diminished	Neg.
31	Pvt.	29	Amer.	Railroad brakeman	No diabetes, mother obese	Mumps and typhoid as child	1 1/12 overseas. Fractured 3 metatarsal bones	Two months	Immediately, but high diets caused persistent glycosuria.	6 ft. 1 in.	185	150	140	Negative	Negative	General adenopathy	Negative	Neuritis of 11th right intercostal nerve	Neg.
32	Pvt.	23	Amer.	Teamster	No diabetes or obesity	Mumps and pneumonia as child	6/12 not overseas	Two weeks	Immediately	5 ft. 10 in.	160	140	138	Negative	Chronic tonsillitis	Negative	Negative	Negative	Neg.
33	Pvt.	27	Irish	Machine work	No diabetes or obesity	Mumps and measles as child	6/12 not overseas	One and one half months	Immediately	5 ft. 5 in.	140	112	110	Caries, 2 abscessed	Chronic tonsillitis	Negative	Ptotic abdomen, bradycardia	Knee-jerks increased	Neg.
34	Corp.	27	Amer.	Foundry work. No lead	Maternal family obese. No diabetes	Measles as child. Scarlet 6 weeks prior to admission	1 overseas	Four months	Immediately; treatment broken by lack of facilities on transport	5 ft. 10 in.	145	140	130	Negative	Negative	Palpable cervicals	Negative	Negative	Neg.
35	Pvt.	28	Jew	Printer	No diabetes or obesity	Measles as child	6/12 not overseas	No symptoms; discovered in routine examination	Immediately	5 ft. 5 in.	115	100	100	Negative	Negative	Negative	Negative	Negative	Neg.
36	Pvt.	26	Negro	Farmer	Father obese. No diabetes	Measles and malaria as child. Mumps Oct. 6, '18. Gonorrhea 9 yrs. ago	10/12 not overseas	One month	Immediately	5 ft. 7 in.	142	137	130	Negative	Chronic tonsillitis	Palpable cervical and epitrochlears	Negative	Negative	Neg.
37	Pvt.	25	Greek	Cook's helper	No diabetes or obesity	Denies all diseases	11/12 not overseas	Existed prior to military duty, discovered two months after induction	Immediately	5 ft. 10 in.	140	110	...	Extensive caries and pyorrhea	Chronic tonsillitis	Negative	Emaciation, dyspnea, very weak; no organic trouble found	Knee-jerks diminished	Neg.

Case No.	Symptoms. Glycosuria.	Acetonuria.	Plasma sugar %	Plasma CO_2 combining power vol. %	Clinical.	Stay in hospital months.	Maintenance diet. Protein.	Carbohydrate.	Calories.	Faithful to diet.	Other treatment.	Plasma sugar under treatment.	Prognosis and reasons.	Remarks.
27	Moderate	Negative	0.192	63.3	Polyuria; polyphagia; polydipsia; loss of weight and strength; ankle edema	4	70	40	1500	Yes	None	0.192–0.09	Bad. Latent tuberculosis and continuous acetonuria	*X*-ray corroborates physical finding at left apex.
28	Negative	Faint	0.150	....	Polyuria; polyphagia; polydipsia; general malaise	3	80	50	1400	Yes	None	0.15 –0.125	Fair. Persistent acetonuria, requires further treatment	Patient failed to gain weight while convalescing from acute icterus following gas.
29	Faint	Negative	0.117	....	Polyuria; polyphagia; polydipsia; loss of weight and strength	2	70	40	1800	Yes	None	0.117–0.10	Good. Intelligent and trustworthy	
30	Heavy	Heavy	0.375	....	Polyuria; polyphagia; polydipsia; loss of weight and strength	4	80	10	1000	No	None	0.375–0.115	Bad. Ignorant and untrustworthy	
31	Heavy	Moderate	0.400	....	Polyuria; polydipsia; polyphagia; loss of weight and strength	2½	80	40	1500	No	Physiotherapy	0.400–0.105	Bad. Ignorance and poor environment	
32	Heavy	Faint	0.221	....	Polyuria; polydipsia; polyphagia; slight loss of weight	2	80	20	1200	No	None	0.325–0.100	Bad. Ignorant and untrustworthy	
33	Negative	Faint	0.15	....	Polyuria; polydipsia; blurred vision; loss of weight and strength	3	80	40	1200	Yes	None	0.154–0.09	Fair. Ignorance may be overcome in institution	Electrocardiogram shows sinus bradycardia. Eye-grounds suggest beginning retinitis.
34	Moderate	Negative	0.210	....	Polyuria; polyphagia; polydipsia; loss of weight and strength	1	80	40	1500	Yes	None	0.210–0.11*	Fair. Intelligence and fair environment	
35	Moderate	Faint	0.147	....	No symptoms	1	80	40	1500	No	None	0.147–0.11	Poor. Ignorance extreme	Glucose tolerance (100 gm). Plasma sugar, % / Urine, vol. c.c. / Urine sugar, % I. 0.115 / ... / (Fasting) II. 0.250 III. 0.326 / 16 / 0.45 IV. 0.272 / 76 / 0.70 V. 0.230 / 140 / Neg.
36	Moderate	Faint	0.297	....	Polyuria; polyphagia; polydipsia; xerostoma	1	80	40	1500	Fair	None	0.297–0.101	Poor. Ignorance and racial characteristics	
37	Heavy	Heavy	0.475	35.0	Polyuria; polyphagia; polydipsia; loss of weight and strength	1	....	....	....	No	None	0.56 –0.06	Bad. Extreme diabetes	Died May 17, 1919.

DISCIPLINE. At first thought a military hospital might be regarded as an ideal place for enforcing rules of diet. Among soldier patients, however, are represented all the usual causes of recalcitrance, such as ignorance, weak will, recklessness, hopelessness of their condition and inclination to end everything as quickly and comfortably as possible by eating to satiety, not only the same as in civilian patients, but also to a greater degree, because a number are included who in civil life would never undertake treatment at all. In addition there are special motives, notably the fact that the patients had no choice, but were sent to take a treatment under compulsion, the grievances already nourished by some against the military service or officers, the habits of enlisted men in grumbling at the quantity and quality of their food, and the natural spirit of sport among them while leading the idle hospital life to see how far they could go in individual or organized disobedience without being detected or punished. Appeal to military law was inadvisable for several reasons: with patients as shrewd and well united as the average soldiers conviction is difficult; the sudden occurrence of glycosuria under fixed conditions is excellent proof of transgression for hospital purposes but not before a military court; pleas that they only ate when forced by extreme hunger would win sympathy and light punishment or none for the offenders; treatment in the guardhouse was impossible unless with solitary confinement; and most important of all, the contention and hostility thus created between patients and officers would ruin the purposes of the service. Accordingly, no patient was subjected to any attempt at arrest or trial, but discipline was maintained by cultivating their knowledge and self-control. They were supplied with the best books and encouraged to find out anything they could through independent reading and inquiries in order to convince them of the seriousness of diabetes and the necessity of dietetic treatment; and at first they were allowed full liberty of movement. When they unanimously and flagrantly broke diet they were confined first to the ward and later to their rooms, not by military guards but by attendants, as in a civilian hospital. Against stealthier violations of diet with protein and fat, substitutions of urine and other familiar tricks, the rule was maintained that blood as well as urine must be constantly normal. Fortunately the first patients had not the severest diabetes, and it was possible to prove to them in confinement that they could be free from hyperglycemia and acidosis on satisfying and appetizing diets. By having the blood-sugar taken at unexpected times they quickly learned that this was a test which they could not cheat or evade. Essentially through the fact that the blood-sugar level decided between food and freedom on the one hand and fasting and confinement on the other, the initial spirit of rebellion died out in about two weeks so completely that it never revived. Thereafter only sporadic individual lapses had to be dealt with, and the general

fidelity was able to meet the two crucial tests of the *esprit du corps* of a diabetic department. One of these is that every patient, without exception, at discharge had feelings of gratitude and the determination (varying with his strength of will) to continue his diet and remain sugar-free outside the hospital. The other is that the patients in the hospital were mutually helpful; the newcomers acquired from the older ones confidence, obedience and knowledge of food values, so that a minimum of instruction or discipline was necessary.

ETIOLOGY. The possible causative influences may be considered under the following headings:

HEREDITY. The record of six patients with diabetic relatives out of a total of thirty-seven is probably higher than would be generally found in an equal number of non-diabetic cases and tends to confirm the existence of a hereditary element, especially if it be conceded that some instances were probably missed on account of the ignorance of many of the patients concerning their family history. The family incidence of obesity, tuberculosis and neoplasms is probably rather high, though exact reckoning is unprofitable for the above reason. The remarkable hereditary features of Case No. 15 furnished the subject of one of the special papers referred to previously.[3]

RACE. The proportion of two Jews and three Negroes was unusual. More of the former and fewer of the latter would naturally have been expected. The relation may have been accidental and the statistics for the entire army may be very different. Otherwise nothing special was noticed in the racial incidence.

CHARACTER AND CONSTITUTION. Patient No. 37 was mentally inferior.[4] The others were fully up to the average of soldiers mentally and physically, and, on the whole, were of an excellent type in both respects. The experience tends to discredit the idea of general constitutional defects in diabetics.

DIET. Neither excess in carbohydrate nor general gluttony was apparently more prominent in these patients than among the average population, and there was no evidence of diet as a primary cause in any case. If patient No. 1 had eaten less the development of his diabetes would presumably have been delayed or perhaps prevented, according to the known rules of treatment, and the same may be true of the others in proportion to their obesity and habits. In the majority of the series overeating was not evident even as an exciting cause, and the proportion of thin and abstemious patients equalled or exceeded that of fat and gluttonous patients. In general, such observations will perhaps hold more strongly for young persons than for the more elderly type of diabetics.

NERVOUS CAUSES. No soldier in this series was markedly neurotic and the great majority were strong and well poised, sometimes phlegmatic. The high proportion of nine officers to twenty-eight

enlisted men is probably artificial, because the urine of officers was examined more often, and they were more likely to come for special treatment. Thus, one of the officers was not from the army but from the navy, and some of the others had made special efforts to be transferred to Lakewood. The greatest advantage of such a service in regard to the theory of the subject lay in the opportunity of observing possible cases of diabetes following physical or psychic shock, strain or injury. Only one case was encountered in which the onset of glycosuria seemed, with considerable probability, to date from a tremendous shock, and this proved to be renal glycosuria. Patient No. 22 was gassed with mustard and chlorin and a few hours later suffered concussion from a high-explosive shell. He was sent to a field hospital on account of "nervousness and excitement" and thence to a rest camp, in which clinical symptoms of diabetes were noticeable for the first time and the diagnosis was made by urinalysis a few weeks later. The most probable assumption is that a diabetic predisposition existed in such a case, and the lack of prior urinalyses prevents decision whether the shock came before or after the beginning of the glycosuria and concerning its role in the causation. Two other patients had histories somewhat like this one. No. 8, the naval officer, was on a torpedoed vessel and suffered from anxiety and exposure, though not wounded. No 3, a captain of artillery, sustained head injuries in a motorcycle collision at the front, and a month later was blown up by the explosion of an ammunition dump from which he was trying to rescue a wounded comrade. Glycosuria and other diabetic symptoms followed in each case, but it happens that in each of these the existence of diabetes was known before the injury. Even an aggravating influence of the shock is not established, for in the former instance the improper diet on reaching port sufficiently explained the outbreak of symptoms, and in the latter case the diabetes remained mild, as it had been before. Wounded or sick soldiers were the ones most often subjected to urinalysis, and it was therefore natural that the diagnosis should often be made at such a time. Thus, patient No. 31 fractured three metatarsal bones during debarcation in France, and diabetic symptoms and glycosuria were noticed shortly thereafter. On the other hand the rarity of glycosuria after injuries is the striking lesson of the war. Also a large number of glucose tolerance tests performed by various medical officers for various purposes upon men returning from overseas suffering or convalescent from medical or surgical conditions have shown no special diabetic tendencies. If such tendencies were created in any marked degree by any form of injury, shock, strain or suffering, it must inevitably have been revealed by the observations on a wholesale scale in the different armies and even the civil populations. The war has been in this respect an immense experiment on human beings, establishing firmly some conclusions which could scarcely have been settled by

animal experimentation. While nervous influences are not excluded as affecting diabetes when the disease or predisposition is present, the main contribution of the war to this subject is the fact that the epidemic of diabetes which was to be expected on the nervous hypothesis of the etiology did not occur, and consequently this hypothesis, as concerns the primary cause of the disease, is decisively overthrown.

Syphilis. This infection was demonstrated in 4 of the 37 cases. Patient No. 3 had a definite history, strongly positive Wassermann reactions in blood and spinal fluid and early paresis. No. 8 had first a negative Wassermann in the blood, later a one plus after a provocative dose of salvarsan, a two plus (army nomenclature) in the ascitic fluid and a cirrhosis of the liver which responded markedly to specific treatment. No. 16 had a history of a chancre in 1908 and double plus Wassermann tests in the blood in that year and 1915. His diabetes was discovered following circumcision in 1915 and progressed downward notwithstanding military treatment, which made his blood Wassermann negative, the test being also found negative in the spinal fluid. No. 23, a Negro, had a history only of gonorrhea and no symptoms or signs except a two-plus Wassermann reaction. No. 22 was reported to have a one-plus blood test, but the negative findings in all other respects were accepted as excluding syphilis. Careful examinations gave no grounds for suspicion in the other 32 cases.

Other Infections. Matters as trivial as an occasional small cavity in a tooth are omitted from the table. The dental service found small root abscesses in 6 cases. The extremely bad teeth of patient No. 37 may have had etiological importance.[4] The 17 cases of chronic tonsillitis tabulated are mostly technical diagnoses, which did not cause the throat department to advise tonsillectomy and can scarcely serve to incriminate the tonsils. The personal histories of the patients, as a whole, included about the usual list of miscellaneous infections. In 7 cases suspicious events antedating the diabetes were elicited as follows: No. 7 had malaria and "tropical liver" in 1906, and the liver is still enlarged; diabetes was discovered in September, 1918, and became worse with influenza the following month. No. 9 had appendicitis with peritonitis and operation in April, 1917, passed examination (with urinalysis) for commission in November, and the first symptoms and diagnosis of diabetes occurred in May, 1918. No. 12 contracted acute tonsillitis at the front in May, 1918, and diabetes followed immediately. No. 14 had "grippe" in October, 1917, followed immediately by diabetic symptoms. No. 21 had influenza and pneumonia, followed immediately by diabetic symptoms. No. 23 (Negro) likewise had a respiratory infection, returned to duty after two weeks, felt weak and after seven weeks was forced to enter the hospital, where diabetes was diagnosed. No. 28 had pneumonia at fifteen and several attacks of

jaundice since. In October, 1918, he inhaled a little mustard gas and immediately developed jaundice, clay-colored stools and tenderness in the gall-bladder region, followed within two weeks by diabetes. Such histories are very suggestive, especially in view of their number; but the same care must be used as in the judgment of trauma and shock, and these cases can never be fully conclusive for the same reasons. In several cases of this series, dental caries and pyorrhea, boils, influenza and other infections are known to have followed the onset of diabetes, in conformity with the familiar lowering of resistance in this disease; and in case No. 34 the history of scarlet fever six weeks before admission seemed significant until it was found that the diabetes was of four months' duration. Also the above-mentioned fact that the sick most often have their urine examined, and the aggravation of an existing diabetes which is known to result from infection may likewise serve to explain the observations of both glycosuria and other symptoms under these conditions. The decision is governed chiefly by pathological evidence[5] that the origin of diabetes is regularly in an infectious pancreatitis. Infections of the above character thus acquire significance as the causes of such pancreatitis, and also syphilis, which is known to cause pancreatitis, is easily understood as a cause of diabetes in certain cases. The combination of the above 7 cases and the 4 luetic cases makes a high proportion of cases in which the infectious origin is directly suggested. It so happened that in Case No. 21 the assumed pancreatitis could be verified by autopsy, and the same pathological basis was also found in the two other cases which came to autopsy. It may therefore be concluded that the origin of military and civil diabetes is the same.

Type of Cases. There was some expectation that soldiers would furnish a selected group of cases of recent onset in young persons. The severe type characteristic of the young did in fact predominate, but the chance to treat such cases in their earliest and most hopeful stage was seldom obtained. Some diabetics were accepted in the draft and in others the diagnosis and treatment were delayed surprisingly long, as shown in columns 9 and 10 of the table. On the whole the cases were about the same as an average group at similar ages in civil life. Stated otherwise, this means that doctors overlook diabetes to about the same extent in military and in civil practice, and that in general the lack of early diagnosis is the greatest obstacle to the attainment of the best therapeutic results.

Treatment. All discoverable abnormalities were treated as in normal persons; carious teeth were filled or extracted; arsphenamin, mercury and iodides were used in the luetic cases and tonsillectomy was performed in case No. 12, which began with tonsillitis. As usual a probable cause of downward progress was thus removed, but

[5] Rockefeller Institute monograph No. 11, 1919, Chapter VIII.

in no instance did the diabetes run a course different from the average thereafter. As permanent damage has generally been done in the pancreas it is unreasonable to expect a cure of diabetes by removal of the infectious cause. The diabetes was treated by initial fasting until glycosuria ceased, followed by a diet of protein and generally a little carbohydrate until hyperglycemia and acidosis were abolished. The diet was then built up, especially with fat, as shown under "maintenance diet" in the table, the allowance of all three classes of foods being governed by the severity of the case and normal blood-sugar and negative nitroprusside reactions being insisted upon throughout.

RESULTS. Mention should first be made of the 5 deaths, 3 in hospital and 2 outside. Patient No. 15 had advanced tuberculosis and acidosis at admission, improved temporarily and died after five months.[3] No. 21 entered with a middle-ear abscess and died of meningitis before the diabetes was thoroughly under control. No. 37 was an extraordinary case in which the diabetes could not be controlled by fasting.[4] Patient No. 13 was a hopelessly weak-willed individual who improved during three months in hospital but required confinement most of the time; he was discharged into bad environment, made a brief attempt to continue diet, then ate at will and died within three months. No. 17 had inherently very severe diabetes, but in conduct was one of the best in the series; after four and one-half months in hospital, during which he was in excellent condition, he was discharged with a good prognosis and died within two months. The danger lay in allowing such a patient to live far away from the supervision of any specialist. The terminal symptoms of nausea and collapse suggest fasting acidosis, and the boy possibly overstepped his diet unintentionally and encountered disaster when he tried to check symptoms by fasting.

RESULTS CONCERNING COMPLICATIONS. The fatal ending of tuberculosis and middle-ear abscess was mentioned above. Otherwise complications have ended favorably or failed to develop. Tonsillectomy was safely borne and every patient has responded to dental or surgical treatment like a normal person. During the extensive influenza epidemic it so happened that no diabetic patient acquired it, though they were equally exposed with other patients. The freedom from the traditional tormenting complications of diabetes is one of the principal benefits of thorough treatment, and the higher resistance to infection of the patient kept symptom-free by undernutrition as compared with the one who has active diabetes is a point to be emphasized.

RESULTS CONCERNING DIABETES. With the exceptions mentioned it was possible to attain freedom from hyperglycemia and acidosis in all cases and to maintain this freedom on a diet supporting the body weight at a level inversely proportional to the severity of the case. The few cases in which the table shows a "mainte-

nance diet" of only 1000 to 1200 calories were some in which diet had been broken so that treatment was not complete at discharge, though they were not more severe than some others. It is recognized that in cases more severe than these the standard of treatment mentioned sometimes necessitates extreme emaciation and weakness if the attempt is to be made to prevent downward progress by keeping the diet strictly within the assimilative power. These distressing end-stages may be either prevented or postponed by application of the same principle in the earlier stages, and for this purpose it will be noted that the diet in even the mildest cases was fixed so as to maintain a reduced level of weight.

PROGNOSIS. Notwithstanding the general favorable progress in hospital the prognosis is recorded as unfavorable in a high proportion of the cases. It unfortunately is still unproved whether the best treatment by the present methods can succeed permanently in arresting the downward progress in severe cases. But when poorly educated patients must go out to make their living in unfavorable environment without proper supervision, the result can be easily foretold. Unsuccessful attempts were made to interest the Red Cross and other organizations in establishing some institution or colony for the after-care of such patients, whose fate is typical of the neglect of chronic disease among the poorer classes in most communities.

STUDIES IN BONE GROWTH: AN EXPERIMENTAL ATTEMPT TO PRODUCE PSEUDARTHROSIS.

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ASSISTED BY

HAROLD F. MORRISON, FIRST LIEUT., M.C., U.S.A.

THE studies herewith presented, and others which will be published later, were made possible through the generosity of the Surgeon-General in permitting the addition of a well equipped animal research annex to the pathological laboratories at U. S. Army General Hospital No. 3, Colonia, N. J., thereby affording facilities for the continuation of investigations relative to bone growth and allied subjects.

In the early months of our participation in the War, during the preliminary organization of this hospital under the joint auspices of the Red Cross and the Surgeon-General's Office, the author, who had been designated as director of the hospital, was allowed to draw

the plans of the laboratories to include not only the usual pathological and bacteriological departments, but a completely equipped animal research annex. As a result of a conference with Colonel F. F. Russell, M.C., Chief of the division of laboratories, privileges were granted which anticipated the work included in this paper by making ample provisions for further research in bone metabolism.

U. S. Army General Hospital No. 3 was opened for the treatment of surgical cases in the summer of 1918, the first patients being admitted early in July, 1918. En passant, it is of interest to note that of all the hospital units whose preliminary organization was made under the Red Cross, in conjunction with the Surgeon-General, this institution was the only one to be ultimately established as a military hospital in this country.

The laboratory, as planned at U. S. Army General Hospital No. 3, included animal houses, animal operating-room and animal autopsy-room, as well as the usual departments of the clinical sections of the laboratory, namely, large chemical, bacteriological and pathological rooms. Coincidently with our clinical bone work, research in various allied problems was made since the early days of the hospital's establishment. These experimental studies were carried on under the auspices of the Surgical Service, with the close and efficient coöperation of the laboratory staff.

Such resources in equipment and technical assistance permitted the continuation of investigations especially desired by the author; foremost among which were an experimental study of the etiology of pseudarthrosis and an attempt to discover some trustworthy artificial stimulus to osteogenesis. This research was carried on with the object of supplementing earlier investigations,[1] made about ten years ago at the Cornell Animal Hospital, which dealt with various phases of bone growth, such as the experimental fusing of dogs' vertebræ by means of the inlay graft, and studies of the relative osteogenesis of bone obtained from various portions of dogs' and rabbits' anatomy. It was found at that time that cubes of bone removed from the spinous process of a vertebra were much less active osteogenetically when placed in a muscle belly, than were cubes of the same size taken from the shaft of a dog's long bone, thus proving the advisability of employing the bone graft for fusing the vertebræ in such conditions as caries of the spine, compression fractures of the vertebral bodies, selected cases of scoliosis, et cetera.[2]

Other experimental investigations were made at that time concerning the relative osteogenetic properties of the periosteum when

[1] Albee, F. H.: An Experimental Study of Bone Growth and the Spinal Transplant, Jour. Am. Med. Assn., 1913, lx, 1044–1049.

[2] The lowered osteogenetic potency of the spinous processes of the vertebræ, largely due to their meagre periosteum and excess of ligamentous attachments, was clearly demonstrated by these experiments. Therefore, in attempting fusion of the vertebræ, it is more trustworthy to inlay a bone graft which thus supplies the needed osteogenetic activity at the same time that internal fixation is produced.

secured by *scraping the outer surface of the bone* with a sharp instrument, as compared with the osteogenetic power of the outer portion of the periosteum when obtained by means of *separation through the easier line of cleavage* with the use of a blunt instrument. In the first instance, the *complete* periosteum was obtained, and this was found to be a very potent osteogenetic element, whereas, in the latter case, osteogenetic activity was found to be only localized in those spots where portions of the cambium layer (which, alone, contains the active bone-growing cells) happened to come away with the so-called "limiting membrane" of Macewen. Studies were also continued which bore out the inadvisability of attempting the transplantation of bone tissue from one species to another, such as the grafting of sheep's bone into a dog, or dog's tissue into a rabbit. These latter findings, it is believed, bear very materially upon the ruling out of any attempts to transplant animal bone into the human subject and the advisability of always using, when possible, autogenous graft material.

Our bone research work at U. S. Army General Hospital No. 3 included an experimental study of pseudarthrosis, with a special object of determining the influence, if any, exerted by the roentgen ray upon callus formation. Another purpose of our investigations was to discover some trustworthy artificial stimulus to osteogenesis. A report of these latter findings will be published by the author at an early date.

The first experimentations at this hospital were carried on in an endeavor to ascertain, if possible, the etiological factor in pseudarthrosis, or malunion. One has but to observe the vast amount of literature written on the subject to realize the surgical importance of this condition. Whether the ever widening interest in this unfortunate malady is indicative of an actual increase in its prevalence, under our modern methods of living, is open to debate. The experience of the author, during the past fifteen years, would certainly bear out the impression that pseudarthrosis is on the increase. This conclusion has been strengthened by discussion with many colleagues likewise interested in bone work. In this connection, a Canadian surgeon recently assured the author that, in his opinion, change of diet necessitated by the Great War was the cause of the very large increase in such cases in his own practice. Among the many factors[3] to which has been attributed a possible role in the causation of pseudarthrosis, special attention has been given to the following:

1. *Method of Splinting.* A consideration of influences possibly favoring the production of pseudarthrosis has included the type of splint and its adjustment in relation to interference with normal circulation; the length of time that the splint should be worn; the proper time for instituting massage; the type of coaptation splints; and the value of traction.

[3] In passing wholly from clinical experience, it is the opinion of the author that syphilis has been greatly overestimated as a cause of this condition.

2. *Diet.* As referred to above, diet has frequently been discussed as a possible cause, in its relation to sluggish bone growth.

3. *Location of the nutrient artery*, with respect to the fracture, and the possible interference therefrom with the blood supply to the region of the fracture.

4. *Presence of Systemic Disease.* Lues, or atrophic conditions, such as neuro-arthropathies, etc., have been considered, in their influence upon bone metabolism.

5. *The Internal Application of the Metal Plate.* From the author's clinical experience, this would appear to be one of the most frequent causes of pseudarthrosis. In this hospital, there have been a goodly number of cases of malunion, without loss of bone substance, all of which have occurred in young soldiers, averaging unusual good health. In a large percentage of these cases, metal plates had been previously applied.

6. *The Roentgen Ray.* It is an established fact that repeated massive exposure to the roentgen ray is a potent inhibitor to cellular growth, in reference to spermatozoa, etc.

Of all the influences enumerated above, that of the roentgen ray is the only one which has been markedly increased within the last decade. In a modern bone clinic, it is, indeed, a rare exception when a fracture is not subjected many times to radiographic examination. The remarkable increase in prevalence of pseudarthrosis coincident with the coming into common usage of the roentgen ray presents a possible correlation. In a consideration of factors contributing to the causation of pseudarthrosis, it seemed, therefore, to the author that the influence of the roentgen ray should be one of the first to be investigated.

In our studies in bone growth, rabbits were selected as the experimental subjects. Young to middle-aged adults were chosen, no animals of either age-extreme being used. Careful asepsis was invariably observed, the field of operation being always treated with a 3½ per cent. tr. iodin preparation. In our entire series of cases, numbering over 80, together with controls, there were but 2 instances of infection. These both occurred in the earlier studies in pseudarthrosis, and were in cases of compound fracture of both bones of the foreleg.

In the majority of our early experiments, it was our method to fracture both bones of the foreleg, an external splint being then applied for fixation and support. The numerous contrivances which are employed for such purposes vary widely in efficacy and cost.[4]

[4] While studying methods of rehabilitation in Canada, the author was especially impressed with one type of splint that was shown him at a certain institution. It was a rather complicated, hinged device, of aluminum, consisting of several parts riveted together, and was manufactured at that hospital in a shop specially organized for the purpose.

The contrast, in cost of material and of manufacture, between this splint and one about to be described is worthy of consideration.

In an attempt to secure an adequate splint for the rabbit's leg, one that would at once maintain immobilization of the fractured fragments, as well as prevent the animal from gnawing its foot, the following extremely simple method was devised of producing an efficient splint:

A piece of copper wire mosquito-netting, 3″ x 6″, is placed on a pine board with the center of the netting square directly over a hole, $\frac{5}{8}$ inch in diameter, through which by means of a blunt soft pine plug, the netting is driven by a mallet and moulded into a cylinder, one end of which is closed. By trimming with the shears, the desired length is secured.

FIG. 1.—Splint for rabbit's leg—a simple and efficient device for maintaining immobilization of the fractured fragments, and one which will prevent the animal from gnawing its limb. This splint is made of copper wire mosquito-netting in the manner shown in Fig. 2. It is trimmed to the desired length and held in place by means of narrow strips of adhesive plaster.

After painting the line of sutures with 3½ per cent. tr. iodin and application of the proper gauze dressing to the compound fracture, it was an easy matter to draw this *combination boot and splint* over the animal's leg and to fasten it with narrow strips of adhesive plaster (Fig. 1). Animals splinted in this manner were less able to injure their limbs or interfere with the progress of the experiment. The extreme simplicity of manufacture of such a device (as shown in Fig. 2), together with its minimal cost,[5] seemed to the author additional factors favoring its use.

[5] Computed at the present wartime price of copper-wire mosquito-netting, at 12 cents per square foot, the actual cost of these rabbit splints is a cent and one-half apiece.

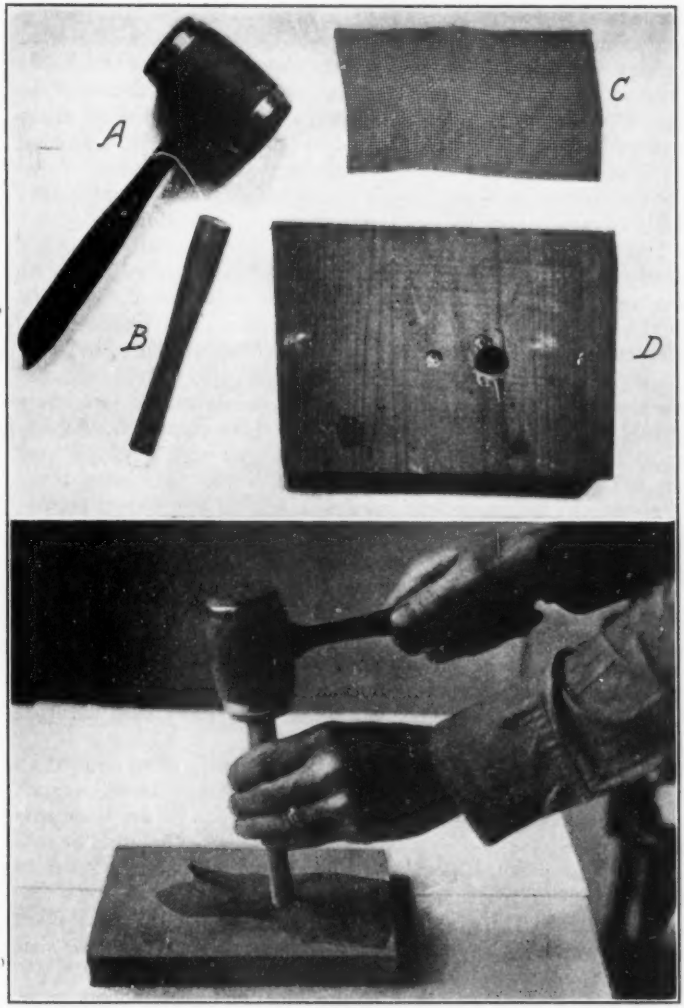

FIG. 2.—In the upper picture are shown the only materials required in the manufacture of the rabbit splint, illustrated in Fig. 1. These consist of a mallet, *A*; blunt soft pine plug, *B*; piece of copper wire mosquito-netting 3″ x 6″, *C*; and a pine board, *D*, which contains a hole ¾ inch in diameter. The copper wire mosquito-netting is placed on the pine board, with its center directly over the hole. Through the hole, by means of the blunt plug, the netting is driven with a mallet and moulded into a cylinder, in the manner demonstrated in the lower photograph. The cost of these extremely simple, but efficient splints, is exactly a cent and one-half apiece.

In the later portion of our series of experiments relative to the etiology of pseudarthrosis, it was found possible to fracture, by open operation, only one of the two bones of the foreleg, the other bone serving as a splint. External splinting was, thereby, avoided. In these cases, it was our method, after careful approximation of the skin edges by interrupted linen sutures, to paint the line of suture well with 3½ per cent. tr. iodin, and to return the rabbit to its cage, without dressing or splint. Animals treated in this manner cared for themselves very well, and it was found that the wound healed quite as rapidly and without the occurrence of infection.

Our first animal experimentations at this hospital, numbering nearly a score, are included in this paper. These studies dealt with the roentgen ray, the removal of various amounts of bone and methods of splinting as possible causes of pseudarthrosis. Detailed reports of these experiments have been omitted, since, in every instance, the same result was obtained, namely, prompt union of the fractured fragments, usually with ample callus formation. Briefly summarized, our investigations and results were as follows:

(*a*) In one series of cases, sections of bone were removed from the radius, leaving a hiatus of considerable size, care being taken to remove *all* the small bone fragments. In every instance, prompt union by ample callus formation occurred.

(*b*) A second series of the same type of case as the foregoing, was then subjected to repeated long exposures to the roentgen ray; these cases likewise promptly united.

(*c*) A series of the same type was also splinted, as adequately as possible (see Fig. 1), and in other cases, no splint whatsoever was applied, the other bone of the foreleg being relied upon for support and to secure general alignment. Union in every case occurred promptly.

(*d*) In another series of cases, bone fragments were allowed to remain in the hiatus; as was anticipated, these cases showed a much more rapid bone growth than did those in which all the fragments were removed. Union occurred promptly, whether splinted or not, and whether or not subjected to massive and frequent exposures to the roentgen ray. Attention should be drawn to the clinical value of these observations which demonstrate the advantage of leaving *in situ*, whenever possible, attached fragments of bone in comminuted fracture, rather than removing them, as is frequently done by surgeons who do not grasp the fundamental laws of bone growth.

Following the suggested role of the roentgen ray as a possible factor in the etiology of pseudarthrosis, an experimental test of such a possibility was made on a series of cases. In each instance, after removal of ¼ inch of bone from the shaft of the right radius, the rabbit was subjected to massive roentgen-ray exposures at intervals of about five days, 5-inch gap, 3½ ampères, being used for five minutes. As controls, the left radii of the same animals were later treated in

like manner, but without massive exposures to the roentgen ray. In the two groups of cases, no appreciable difference was found in the length of time required for union of the bones.

Illustrative of our attempts to produce pseudarthrosis by massive exposures to the roentgen ray, is Case No. 8, which, together with its control, is reported in detail, as follows:

FIG. 3.—Case No. 8.—Second day after operation, showing gap in right radius from removal of ¼ inch of bone. This case was subjected to massive roentgen-ray exposures, 5-inch gap 3½ ampères being used for five minutes. This treatment was begun on the day after operation and continued for 4 successive intervals of about five days.

FIG. 4.—Case No. 8.—Twenty-five days after operation, showing evidence of a slight degree of bone growth. This radiograph was taken five days after the last of the series of massive roentgen-ray treatments.

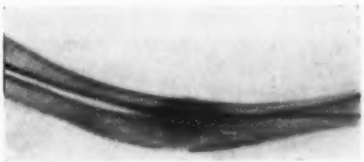

FIG. 5.—Case No. 8.—Forty-three days after operation, and about three weeks (twenty-three days) since last massive roentgen-ray treatment. Union is complete. Note that this radiograph shows more active bone growth and a more complete union than its control on which the roentgen ray was not used, save for short exposures in order to note progress of union.

CASE No. 8.—Subject, common hare.

March 20, 1919. Fragment of bone, one-quarter inch in length, removed from shaft of right radius.

Exposures to roentgen ray.

March 21. Subjected to 5-inch gap, 3½ ampères, for five minutes.

March 25. Above treatment repeated.

March 30. Above treatment repeated.

April 4. Above treatment repeated.

April 9. Above treatment repeated.

Radiographic findings:

March 22. Second day after operation, roentgen ray shows gap of ¼ inch in shaft of radius. (See Fig. 3.)

April 14. Twenty-five days after operation. There is evidence of a slight degree of bone growth. (See Fig. 4.)

May 2. Forty-three days after operation—complete union is shown. (See Fig. 5.)

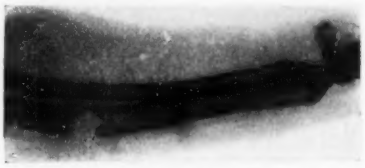

FIG. 6.—Case No. 8*a*.—Control of Case No. 8. Second day after operation showing ¼ inch gap in left radius. This case was not subjected to massive roentgen-ray exposures.

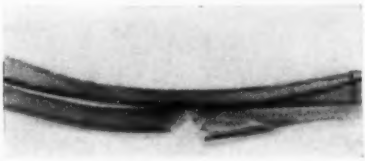

FIG. 7.—Case No. 8*a*.—Twenty-five days after operation. There is some evidence of bone proliferation.

FIG. 8.—Case No. 8*a*.—Forty days after operation, showing union of fragments. Compare with case No. 8, Fig. 5.

CASE No. 8*a*.—Control of Case No. 8.

A fragment of bone, one-quarter inch in length, was removed from the shaft of left radius.

Radiographic findings:

1. Second day after operation—roentgen rays shows gap of one-quarter inch in radius. (See Fig. 6.)

2. Twenty-five days after operation. There is evidence of a slight amount of bone proliferation. (See Fig. 7.)

3. Forty days after operation, union of fragments is shown. (See Fig. 8.)

In the foregoing experiments, it was found that bone growth was in no degree inhibited by the use of the roentgen ray. In fact, in Case No. 8, after a series of five massive exposures, complete union was shown forty-three days after operation, and proliferation even greater than occurred in its control on which the roentgen ray was not used, save for short exposures in the aim of obtaining radiographic findings. (See Figs. 5 and 8.)

It not infrequently results that a pure investigator, working along laboratory lines and not meeting clinical problems, goes far astray, and, in some instances, an excellent piece of research has come to naught owing to the fact that it was founded upon false premises. Illustrative of this is a report[6] of animal experimentation with fragmented bone grafts, recently published, in which that author introduces his paper with the following erroneous statement, as a premise:

"The bone (forearm) is too small to maintain a transplant in position by the use of a Lane plate or other device; and the insertion of an intramedullary splint with a dowel is a procedure of considerable difficulty and requires a large exposure of the fractured bone. In performing bone transplant operations in dogs while pursuing the study of bone repair, the writer was struck with the universally good results obtained by transplanting small bone fragments 1 to 2 mm. in size, to fill a defect in the shaft of the radius. Although this study is purely an experimental one, it is reasonable to assume from the results obtained that it will be of distinct clinical value in well selected cases."

The first statement, namely, that "the bone is too small to maintain a transplant in position by the use of a Lane plate or other device," is an unfortunate suggestion, since the Lane's plate should *never, under any circumstances,* be used as the fixative agent for the graft. The intramedullary splint, it is true, is not applicable in these cases; it is, however, an indisputable fact that the inlay graft, when properly inserted, affords an ideal fixation and an exceedingly promising prognosis. The most unfortunate part of that author's premise is his statement that, because by his method of placing small bone fragments in a hiatus freshly made in an animal's long bone, union was produced, it would be "reasonable to assume from results obtained that it would be of distinct *clinical* value in well selected cases,"[6] in the treatment of pseudarthrosis.

The error of such conclusions, as the foregoing, can be no better emphasized than by a summary of our results obtained with rabbits in our attempt to determine the cause of pseudarthrosis. In our experimentations, we failed absolutely to produce a single case of pseudarthrosis, simply because we were unable to prevent the early

[6] Bancroft, F. W.: The Use of Small Bone Transplants in Bridging a Bone Defect, Ann. Surg., 1918, lxvii, 457.

and rapid union of the fragments of the shafts of the long bones. In one series of our cases, discussed above (see *d.*), bone fragments were allowed to remain in the hiatus in precisely the same manner as described in the article quoted. Union in these cases, as has already been stated, occurred promptly whether the shaft fragments were splinted or not, and whether or not subjected to massive and frequent exposures to the roentgen ray. It is, thus, clear that the experimental findings, as set forth in the article above cited, can have no force, whatsoever, as argument for the *independent* use of osteoperiosteal grafts, in the clinical treatment of genuine pseudarthrosis, or malunion.

On the other hand, no one is more strongly convinced of the potency of fragmented, or osteoperiosteal, grafts as producive of bone growth, than the author, who, in experimental work as early as 1909 and 1910,[1] observed the unusual osteogenetic activity of such transplants. It is of interest, in this connection, to make reference to Case No. 5 (see Figs. 9 to 12), of our series of experimentations herewith reported. In this case, one slender fragment of bone was left in the hiatus formed by removal of about one-quarter inch of substance from the shaft of the radius. In striking contrast to those cases in which *all* particles of bone were removed from the gap at first operation (see Cases No. 8 and 8*a*, Figs. 3 to 8), this case showed a remarkable and rapid bone proliferation at the end of twenty days. Furthermore, by the thirty-first day, not only was there complete and solid union, but the gap was entirely filled with new bone. In cases in which all fragments were removed, a period of about forty-two days seemed required for union. The remarkable osteogenetic activity manifested in Case No. 5 was, of course, due to the presence of additional bone surfaces containing the potent bone-growing cells, namely, the fragment which originally remained, spanning the hiatus in the shaft of the radius. This bridge of bone functionated in the identical manner of an osteoperiosteal, or fragmented graft.

The value of the osteoperiosteal, or "sliver" graft, as a means of furnishing further foci for bone growth, has been repeatedly demonstrated, not only in the author's animal experimentations, but more particularly in the application of these grafts as supplements to the main fixation graft in his series of nearly 2000 cases of bone transplantation on the human subject. However, emphasis should be laid on the fact that in all clinical cases of pseudarthrosis, with or without loss of bone, such grafts should be employed *only as supplemental* to the main fixation graft which must be so inserted as to lie in generous contact with the primary source of blood supply and nourishment to bone, namely, the marrow cavity, or the cancellous bone structure. This can only be satisfactorily accomplished by the inlay method. The definite limitations to the use of fragmented, or osteoperiosteal, grafts have never been more convincingly demon-

strated than by recent reports from American and European surgeons of the failure of these grafts, when used alone, to secure union in cases of pseudarthrosis.

FIG. 9.—Case No. 5.—Five days after operation, showing the removal of about ¼ inch of the shaft of the radius. Note that in this case a slight bridge of bone has remained, spanning the gap between the shaft fragments.

FIG. 10.—Case No. 5.—Twelve days after operation. There is slight evidence of bone growth. (In this figure the film was reversed in printing.)

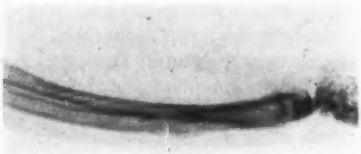

FIG. 11.—Case No. 5.—Twenty days after operation. Note the remarkable proliferation which has taken place. The original hiatus is nearly filled with new bone.

FIG. 12.—Case No. 5.—Thirty-one days after operation. The gap is completely filled with new bone and there is firm union. Compare the progress of bone growth in this case with that of case No. 8 (Figs. 3 to 5) and its control, case No. 8 *a* (Figs. 6 to 8). In both of these latter cases, there was complete removal of all fragments from the hiatus in the shaft of the radius. Note the striking contrast between these latter cases and case No. 5, in their respective radiographic findings. The remarkable osteogenetic activity demonstrated in Case No. 5 was due to the presence of the original bridge of bone left in the hiatus.

Conclusions.

1. In none of our experimentations with rabbits were we able to produce pseudarthrosis by repeated massive exposures to the roentgen ray, by removal of bone, nor by various degrees of splinting.

In every case, even when portions of the radius were removed to the extent of one-fourth of its entire length, we were prevented in our purpose by the early and rapid union of the shaft fragments, it being a well-known fact that bone growth in animals is much more rapid and constant than in the human subject.[7]

2. Frequent, massive exposures to the roentgen ray of fractures, with or without loss of bone, in no wise inhibited callus formation.

Following the suggestion that the common usage of the roentgen ray might play some role in the production of pseudarthrosis, series of fracture cases, with and without loss of bone, were subjected to long and repeated exposures. Comparison with a control group, on which the roentgen ray was not used, save for brief exposures incidental to observation of progress, showed that there was no difference in length of time required for the union of the bones in the two series of cases. Apparently the roentgen ray exerts no appreciable influence upon bone growth.

3. In cases of fracture, with loss of bone, in which *all* bone fragments were removed from the hiatus in the shaft of the radius, the average length of time for union was forty-two days.

Those cases of fracture in which the fragments were allowed to remain in the hiatus, showed a much more rapid and complete union, than occurred in the foregoing group. In one case of fracture, with loss of bone, in which one fragment was left bridging the gap, remarkable osteogenetic activity was manifest, complete restoration of continuity of the shaft occurring at the thirty-first day. This latter case affords a further demonstration of the value of the osteoperiosteal, or "sliver", graft, when used as a means of furnishing additional foci for bone growth.

[7] In this connection, it is worthy of note that in many of the infected cases of fracture, with or without loss of bone, seen in the wards of this hospital, pseudarthrosis occurred, whereas, if the same relative amount of bone tissue be removed from a long bone of a rabbit, regeneration has been fairly rapid and complete.

POINTS IN THE PHARMACOLOGY OF CERTAIN DRUGS USED FOR STOMACH EFFECTS.[1]

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Atropin.[2] This drug has such a decided action on certain secretions and certain motor functions of the body that it has for long years been assumed to have similar effects in the stomach. Yet clinical beliefs that have been supported by the leaders in medicine have so often been forced aside when the light of experiment has been turned upon them, that it behooves us to appraise carefully the value of such a drug as atropin in its application to the stomach.

1. *Secretion.* Observations on human subjects have been made by Crohn with the fractional method of gastric analysis. Some of his results were:

(*a*) *In Hyperacidity Cases with Normal Secretion Period.* One mg. ($\frac{1}{65}$ grain) of atropin sulphate administered to the patient hypodermically three-quarters of an hour after the meal, had little or no effect except that in the last one-half hour there was a rapid *rise* in acidity to 76 at a period when the control showed an acidity of 32. A similar experiment on another patient gave practically the same results. Doses by mouth sufficient to give signs of belladonna-poisoning (dry mouth, dilated pupil, etc.), raised the average acidity from 35 to 51.1. In all cases the motility was unaffected.

(*b*) *In Cases with Continuous Secretion.* In the control test a highly acid gastric juice persisted to the end of the experiment, six and three-quarter hours, though all the food had left the stomach at two and three-quarter hours. After the food had disappeared the acidity was higher than before, reaching 118 at four and one-half hours. The average total acidity was 89.

The next day with the same patient, all food having left the stomach at two and one-quarter hours, 1 mg. of atropin sulphate was given at this time hypodermically, and at one hour later the secretion had ceased. In the same patient fully atropinized by mouth for

[1] Presidential Address at the Twenty-second Annual Meeting of the American Gastro-Enterological Association, Atlantic City, N. J., June 9 and 10, 1919.

[2] Auer and Meltzer: Am. Jour. Physiol., 1906, xvii, 17.
Barclay, A. E.: Alimentary Tract, 1915, p. 17.
Crohn, B. B.: Am. Jour. Med. Sc., 1918, clv, 809.
Cushny, A. R.: Pharm. and Therap., 1915, p. 323.
Ginsburg and Tumpowsky: Arch. Int. Med., 1918, xxii, 553.
Ochsenius, K.: 1915.
Rehfuss, M. E.: Tr. Am. Gastro-Enterol. Assn., 1918, p. 25.
Smith, Maurice I.: Am. Jour. Physiol., 1918, xlvi, 232.
Zunz and Tysebaert: Jour. Pharm. and Exp. Therap., 1916, viii, 325.

three days the stomach was free from food at three hours and the secretion ceased at three and one-half hours. The average total acidity was 60 as compared with an average of 89 in the control, but in this case the averaging of acidities does not make a valid comparison, because in the control the highest acidity was reached during the period of continued secretion, *i. e.*, after digestion was finished, a period in which there was no secretion at all after atropin. In this case exploratory laparotomy had shown no lesion.

In a second case the secretion was still continuous at five and three-quarter hours when the experiment was stopped. The average total acidity had *risen* from 85.3 to 94, the motility being unaffected. Then tincture of belladonna, 1 c.c. four times a day, was given by mouth for three days, when poisonous symptoms appeared. In a test at this time the secretion ceased at three hours, but the average acidity increased from 85.3 to 104.5.

We find then failure of atropin to lessen digestive secretion, and in continuous secretion cases a failure to act except after the digestive period. Then it had an effect only if given by hypodermic in maximum doses, or if previously given by mouth to the stage of poisoning. It actually increased the acidity of the digestive secretion and showed an inhibitory effect only on the abnormal continued post-digestive secretion.

In regard to the psychic secretion I have only the report of Rehfuss. In the early morning each of a number of men with a fractional tube in his mouth was set in front of a beefsteak and compelled to cook it though not allowed to eat it. The stomach secretion, withdrawn at intervals, ceased at sixty to eighty minutes and ran as high a total as 240 c.c., with average acidity of 97.2. In large doses by hypodermic atropin cut down the acidity and the amount of secretion, but never caused complete disappearance of the secretion. It is possible that the drying effect of atropin in the nose, mouth and throat and the sensory effect of blunting the sense of smell may have been important in the result.

2. *Motor Functions.* From a therapeutic point of view the only desired action of atropin on the motor functions is to overcome tetanic spasm at the cardia, at the pylorus and at the site of an hour-glass contraction.

Working with strips from the antrum, pre-antrum, body and fundus of the stomachs of rabbits, cats and dogs, Smith found that solutions of atropin sulphate 1 in 1,000,000 and 1 in 100,000 invariably produced relaxation, whether the strips were from the longitudinal, the circular or the oblique muscles. He obtained the same effects on the pyloric and cardiac sphincters. Zunz and Tysebaert, working on the stomachs of dogs one-half hour after hypodermics of from 0.005 to 1 mg. per kilo, found the contractions weak and diminishing in strength, the effect in some cases persisting five to six hours. After 0.001 mg. per kilo the movements were normal,

though the tone rapidly fell. Auer and Meltzer have demonstrated that these effects are due to paralysis of the vagus terminals at Auerbach's plexus.

I have not worked with stomach strips, but in experiments done with Dr. C. C. Lieb, using strips of the longitudinal muscle of the small intestine of dogs, atropin in large amounts completely abolished the tetanic contraction or cramps brought out by physostigmin and restored the peristaltic waves, but not the normal tone waves. From the work of others it is established that the same action takes place in the stomach. Ginsburg and Tumpowsky, for example, found that hypodermics of $\frac{1}{80}$ to $\frac{1}{40}$ grain invariably in five to ten minutes inhibited the tetanic contraction produced by pilocarpin and physostigmin in the stomach and restored the normal peristalsis. The inhibition was sudden and decisive and persisted for hours. The same results were obtained in the isolated stomach.

This conquering of tetanic spasm by atropin in doses which permit the vagus and splanchnic nerves to continue their ordinary influence on peristalsis has led Cushny to surmise that these abnormal contractions, such as are seen in pylorospasm and colic, arise from some mechanism distinct from that which presides over ordinary peristalsis. This action on abnormal tetanic contractions is indeed *the only possible motor effect of therapeutic amounts of atropin*. It seems therefore essential to distinguish the two known motor effects, viz., that of abolishing abnormal spasmodic contractions and that of abolishing the tone of the whole stomach wall. Only the former is possible or desirable therapeutically, and in all probability it is not accomplished by paralysis of the vagus endings.

Clinically and in roentgen-ray work, atropin has been much employed to overcome abnormal tetanic contractions. On cardiospasm, which it is agreed is not a true spasm, the drug has little or no effect. In röentgenology it is quite generally employed to overcome pylorospasm and the spasm of hour-glass contraction. From fluoroscopic observations, A. E. Barclay reported that after the dose of atropin the spasm often let up quite suddenly, but in some cases the drug was without effect. From a number of roentgenologists I have learned that quite frequently even large doses are without effect on pylorospasm. These men do not use small doses, but are accustomed to the employment of 1 to 1.2 mg. ($\frac{1}{65}$ to $\frac{1}{50}$ grain) of the drug, and that hypodermically, or some of them attempt to atropinize by two or three days' dosage. Within a few weeks I have had a case operated upon for cholelithiasis in which the roentgenologist, finding an hour-glass stomach that did not change after a hypodermic of 1 mg. of atropin sulphate, insisted on a diagnosis of ulcer with cicatricial contraction. But at the operation there was no sign of either hour-glass or ulcer.

In Czerny's pediatric clinic, Ochsenius found that in infants

enormous doses were necessary to overcome pylorospasm. For instance, in one child, a month old, to permit proper feeding, he had to keep up intermittently for ten weeks an atropin dosage of 0.15 mg. ($\frac{1}{435}$ grain) five or six times a day, and in another, three weeks old, had to give the same dose eight times a day for a whole week. There is much evidence of the ineffectiveness in pylorospasm of any but large doses at any age and in adults of the ineffectiveness of any but hypodermic doses; even then the relaxation is frequently not obtained.

Summary. 1. *Acidity and Secretion.* 1. In the ordinary hyperacidity case with cessation of secretion at the usual time, atropin or belladonna in maximum doses, either by mouth or hypodermic, has no useful effect on acidity or secretion.

2. In cases with continuous secretion a maximum dose by hypodermic half an hour before the meal did not lessen the acidity or secretion of the digestive period, but resulted in a stoppage of the secretion in a reasonable time after the food had left the stomach. A similar maximum dose at the end of the digestive period stopped the secretion in one hour.

3. In cases with continuous secretion, repeated maximum doses of the tincture of belladonna by mouth for three days caused a pronounced increase in acidity during the digestive period, but a cessation of the secretion after the food had left the stomach.

4. The psychic secretion is lessened, an effect not sought in therapeutics.

5. The natural secretion of mucus is not affected.

We find then a complete failure of atropin to affect hyperacidity favorably and a failure to diminish secretion except in continuous secretion cases. In these cases it does not depress and may even increase acidity and secretion during the digestive period, and it checks the continuous secretion only when given by hypodermic in maximum doses or when previously given by mouth to the stage of poisoning.

II. *The Motor Functions.* 1. Atropin can exert two kinds of motor effects on the stomach: (*a*) the abolition of tone in the whole stomach wall including the orificial sphincters, by action on the vagus myoneural junctions, and (*b*) the abolition of abnormal spasmodic contractions, as in pylorospasm, this effect probably not being dependent upon any action on the vagus terminals.

2. The latter effect is the only desirable one in therapeutics. It is a possible effect in some of the cases only, and then only from maximum doses.

3. So far as I know the action of atropin on hunger contractions has not been studied.

Conclusions. 1. In hyperacidity cases atropin has no useful effects in any dosage.

2. In continuous hypersecretion cases it may check the secretion after the digestive period, but it does this in maximum doses only.

3. In pylorospasm it may be useful, but in maximum doses only.

4. In the doses usually employed it is wholly without effect on the secretory or the motor unction of the stomach.

PEPSIN.[3] By the U. S. Pharmacopœia test, with 1 in 3000 hydrochloric acid at 125.6° F. (52° C.), pepsin is required to digest 3000 times its own weight of coagulated egg albumen in two and one-half hours, *i. e.*, 1 grain of pepsin can digest at least $6\frac{1}{4}$ ounces. Prof. Gies, of Columbia, tells me that a specimen has been prepared 200 times as strong as this, *i. e.*, 1 grain can digest 600,000 times its weight. What a wonderful substance to have so little use in medicine! It is inactivated by hydrochloric acid above 0.5 per cent. strength (U. S. P.), 0.7 to 0.9 per cent. (Hamburger and Halpern), and by sodium chloride solution of 2.5 per cent. strength. It is not only inactivated but is destroyed by alkalies, for example, disodium phosphate in $\frac{1}{2}$ per cent. strength (Hamburger and Halpern), sodium hydroxide in 0.01 per cent. strength (Sollmann) and sodium bicarbonate and carbonate, magnesium carbonate and lime-water (Hamburger and Halpern), when in sufficient amounts to make a persistent alkaline reaction. In the light of this destruction one wonders how Abderhalden and Meyer were able to find active pepsin in all parts of the small intestine, and to suggest that this pepsin would be active in the digestion of protein wherever the intestinal contents should become acid.

In the stomach contents, Wiltrup found it absent or below normal in every one of a thousand cases of achylia gastrica. Hernando and Alday found it absent in 3 cases and present in only very small amounts in 16 out of 22 cases of gastric cancer and in normal or above normal amounts in 65 cases of hyperchlorhydria, 37 cases of gastric or duodenal ulcer and 85 cases of cicatricial stenosis of the pylorus.

It is evident then that the only possible cases for the use of pepsin in therapeutics would be those of subacidity and achylia, whether cancerous or not. Its need is doubtful, but since pepsin digests protein only when this has been changed to acid albumin, if used at all it should be accompanied by a sufficient quantity of hydrochloric acid.

Pepsin preparations regularly have a milk-coagulating power. Whether this is due to admixture of rennin or because pepsin and rennin are one and the same enzyme is a still unsettled question among physiological chemists.

RENNIN.[4] Rennin is not a digestant, but it has the power to coagulate from 5000 to 166,000 times its weight of milk in from one

[3] Hamburger, W. W., and Halpern, B.: Arch. Int. Med., 1916, xviii, 228.
Hernando, T., and Alday, T.: Siglo Med., Madrid, March, 1917.
Wiltrup, G.: Hospitalstidende, August, 1916.

[4] Harris: Jour. Anat. and Phys., 1894, xxix, 188.

to several minutes. The rennin curd uses up 13 per cent. more calcium phosphate than the curd from hydrochloric acid (Harris) and is less dense and more readily acted upon by pepsin.

The function of rennin in the gastric juice is therefore to retard milk in the stomach by changing it to a solid and to favor the digestion of its coagulable protein.

But in a medium strongly acid or more than slightly alkaline the rennin will not act. Therefore, on the one hand, in hyperacidity cases the curd formed is regularly the dense and comparatively indigestible acid curd and not that of rennin; and on the other the addition to milk of more than a very little lime-water or sodium bicarbonate, or as little as 2 grains of sodium citrate to each ounce will prevent the rennin coagulation, and will keep the milk in its liquid and less digestible form. In highly acid stomachs, however, it may take considerable alkali to prevent the undesirable acid coagulation of milk.

If we add rennin to milk just at the time of swallowing, may we not find this a useful remedy (1) in achylia cases with diarrhea, to coagulate the milk and so prevent its too rapid passage into the intestines, and (2) in hyperacidity cases to forestall the undesired acid coagulation?

HYDROCHLORIC ACID.[5] The known functions of this acid in the normal animal are:

1. To favor protein digestion and the disintegration of connective tissue.
2. To induce closure of the cardia.
3. To establish a normal intermittence of opening and closure of the pylorus.
4. To serve as antiseptic.
5. To aid inversion of the disaccharides.
6. To form secretions to stimulate the production of pancreatic juice and bile.

That the absence of hydrochloric acid is quite compatible with

[5] Arny, H. V.: Practice of Pharmacy, 1918. Crohn, B. B.: AM. JOUR. MED. SC., 1918, clvi, 656.
Ginsburg, Tumpowsky and Hamburger: Jour. Am. Med. Assn., September 30, 1916.
Goiffon, R.: Arch. Mal. de l'Appar. Digest, 1918, ix, 262.
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Jones, N. W.: Am. Jour. Med. Sc., 1918, clv, 335.
Joubert: Quoted by Goiffon.
Leo: Die Salzsäuretherapie auf Theoretische und Praktische Grundlage, Berlin 1908.
Long, J. H.: On the Physiological Activity of Combined Hydrochloric Acid, Investigations of the Therapeutic Research Committee of the American Medical Association, 1915, vol. iv.
Marriott, W. McK., and Howland, John: Johns Hopkins Hosp. Bull., 1918, p. 284.
Rehfuss, M. E.: Jour. Am. Med. Assn., 1917, lxix, 1328.
Spencer, Meyer, Rehfuss and Hawk: Am. Jour. Physiol., 1916, xxxix, 459.
Stehle, R. L.: Jour. Biol. Chem., 1917, xxxi, 461.

fair health and the maintenance of nutrition is proved by the frequency with which the existence of achylia gastrica is discovered after only insignificant symptoms or no symptoms at all. I found achylia present in one girl, aged seventeen years, with complete lack of gastric symptoms, having tested her stomach merely because her grandmother and her mother had shown achylia. For hydrochloric acid as a remedy only one use can be suggested, viz., to replace a deficiency of acid in the gastric juice. Whether introduced acid can so serve is our question.

1. *Protein Digestion.* It is an established fact that for pepsin digestion of protein, acid is necessary. Therefore in an achylia case, if we are to have any digestion of protein in the stomach, we must supply hydrochloric acid as well as pepsin. Experiments done without pepsin regularly show a fair formation of acid albumin and thus give hope that the addition of pepsin may ensure at least some degree of gastric protein digestion.

Crohn, in fractional experiments on man in achylia cases, both simple and those of pernicious anemia, found that it was not possible to have a sustained acidity from mouth doses unless these were frequently repeated during the digestive period. To mention some of his experiments, in an *emptied fasting stomach* he placed 40 minims of diluted hydrochloric acid mixed with 100 c.c. of water. The immediate acidity was: Free 32, total 40. Successive specimens withdrawn at five-minute intervals showed rapidly diminishing acidity until at twenty-five minutes the titer was the same as before the acid had been given. When he administered 30 minims of diluted hydrochloric acid with an oatmeal test-breakfast the free and total acidities at fifteen minutes were 8 and 20 and at thirty minutes 12 and 18, but at forty-five minutes and thereafter had returned to 0 and 10 or thereabouts, the same as in the control experiment.

Then he administered repeated instead of single doses of the acid. Ten minims of the diluted acid every half hour during digestion gave a mild but definite rise in acidity which was sustained for one and three-quarter hours, and 10 minims every quarter hour raised the average total acidity from 20 to 55. The emptying time was unchanged.

Leo, quoted by Crohn, gave achylia cases large doses of hydrochloric acid, equivalent to from 75 to 225 minims of U. S. P. diluted hydrochloric acid, and obtained increases in total acidity but rarely any free acid.

Spencer, Meyer, Rehfuss and Hawk introduced strongly acid solutions (0.542 and 0.4 per cent.), and found that the gastric contents had returned to normal at the end of one hour. This they attributed to a rapid emptying due to the acid and a progressive neutralization of the excess of acid.

Rehfuss found that 10 or 15 minims of hydrochloric acid, properly

diluted, made no detectable change in the gastric chemistry. However, with a constant supply of acid for two hours by a Murphy drip at the rate of 200 c.c. of 0.25 per cent. acid per hour, equivalent to 5 c.c. of diluted hydrochloric acid per hour, the curve of secretion rose to 33 per cent. of normal, though there was at no time any free acid.

All these findings indicate that if we can only give enough hydrochloric acid by mouth, we can at least hope to change our albumin to acid albumin and thus prepare it for pepsin digestion. But acid alone is practically useless for the purpose of digestion, and to judge of its merits as a remedy, it must have all the factors for its action. In other words, we must administer pepsin with it. Moreover, the products of the action of pepsin and hydrochloric acid on protein are themselves capable of exerting a strongly stimulating effect on secretion.

Sippey makes a calculation that for the adult allowance of 100 gm. of protein a day it would require 700 minims of diluted hydrochloric acid for full gastric digestion, and that on account of the sensitiveness of the mouth and throat to acid it would be impossible to swallow this amount. However, there is never, even in normal cases, full protein digestion in the stomach. Moreover, some proteins require less acid than others for digestion, *e. g.*, Hawk states that the best strength for the digestion of fibrin is 0.08 to 0.1 per cent., while the best for coagulated egg-white is 0.25 per cent. Joubert found in achylia cases that on giving hydrochloric acid at the same time as raw meat, connective tissue still appeared in the stools. From strengths of 30 to 40 minims in 100 c.c. of water Crohn noted the development of considerable mucus, presumably from some local irritant action.

2. *The Emptying Time of the Stomach.* That in achylia gastrica it is not infrequent to have a very rapid emptying time is well known. In 11 cases of pernicious anemia, C. P. Horner found that 6 had emptied at one hour and in only 1 was there food at the two-hour period. N. W. Jones in a study of achylia concluded that in a broadly built non-ptotic person achylia is usually associated with a too rapidly emptying stomach and in this class diarrhea is prone to occur; whereas in ptotic types the ptosis and atony prolong the emptying time even up to seven hours or more, and in this class constipation is the rule.

There is considerable clinical evidence that in a fair number of achylic diarrheas, hydrochloric acid is a successful remedy. May not this be due to the restoration of the normal pyloric closure through the acid reflex and the consequent retardation of the food in the stomach? This, it is to be remembered, is a desired effect only in those cases with rapid emptying and diarrhea, and it is to be avoided if possible in those cases with flatulence or constipation. Crohn found the emptying time normal after doses of acid, but he

does not state that any of his cases were of the diarrheal type. Goiffon states that 1.5 to 3 gm. of hydrochloric acid a day may act to cause pyloric closure and so retard the food in the stomach. Jones's experience with the use of acid tallies with that of the author. He says "many are symptomatically relieved by its use, while others experience increased sourness and stomach irritation."

It has been stated that in some achylia cases the diarrhea may be checked by the administration of pancreatin. May not part of the value of hydrochloric acid lie in its power to enhance the pancreatic secretion through the formation of secretin, and thus to ensure more thorough digestion of proteins in the intestines? For though achylia gastrica is not ordinarily accompanied by pancreatic achylia, yet for certainty of digestion the rapidly passed food may require abnormal amounts of the pancreatic ferments.

3. *The Antiseptic Action.* In an achylia case it is quite common to find pronounced intestinal putrefaction. In both diarrhea and constipation cases this may be attributed, in part at least, to the failure of the achlorhydric contents to arrest the development of gas-forming organisms and to destroy the sundry proteolytic and pathogenic germs, thus permitting their passage into the upper intestine. In diarrhea cases intestinal putrefaction might also be accounted for by the fact that the ferments have too short a time in which to break down the protein before it reaches the usual region of abundant germ life in the intestine, and so the protein furnishes pabulum for the bacteria of the colon.

4. *The Effect on Pancreatic Secretion and Bile.* It is a well-established fact that, in the normal case, the hydrochloric acid of the stomach is an important factor in the production of secretin which stimulates the secretion of pancreatic juice and bile. What takes the place of hydrochloric acid in the achylia case, which does not lack pancreatic ferment, has not been determined; but if, from introduced acid, free hydrochloric acid or combined acid, which is really a loosely combined protein salt, can be passed into the duodenum even for a few moments, may not this result in the formation in the normal manner of ample secretin, and so provide the normal stimulus for the production of pancreatic juice and bile?

Summary. In achylia cases, from experiments based on the introduction of hydrochloric acid alone, without its natural congener pepsin, it is evident that with single doses of swallowable strength the acid titer of the stomach contents may be distinctly raised even to the normal. The results that might be expected from this are: (1) Successful protein digestion in the stomach when sufficient pepsin is also introduced; (2) slowing of the emptying time of the stomach by reëstablishment of the pyloric closure reflex; (3) restoration of the normal antiseptic action in the stomach; (4) the proper formation of secretins; (5) normal liquefaction of the stomach contents by the added fluid.

Possible drawbacks to its use are: The establishment of pyloric closure in an already slowly emptying stomach, the production of gastric irritation, and the development of a mineral acidosis from its daily use over long periods of time. That it can produce *acidosis* has been demonstrated in dogs by a number of observers, and recently in man by Marriott and Howland. They gave 500 c.c. of decinormal hydrochloric acid in one day to each of four normal men, who ate their usual diet. This amount would represent 273 minims of diluted hydrochloric acid, a very large amount. On that day there was a distinct increase in the ammonia coefficient in the urine and at the same time an increase in the titratable acid in about the same proportion. Thus in a single day from swallowable amounts in man ammonia was deflected from the usual course of nitrogenous metabolism and a certain degree of acidosis was produced.

Stehle administered hydrochloric acid to dogs by mouth and found an increased excretion of sodium, potassium, calcium and magnesium. In the case of sodium and potassium, however, a subsequent compensatory retention took place. It has been figured that among the other effects there is a loss of calcium from the bones.

It is of interest that Ginsburg, Tumpowsky and Hamburger found hydrochloric acid in 0.5 per cent. concentration to be without effect on the hunger contractions.

Conclusions. 1. In cases of achylia gastrica, whether or not accompanying pernicious anemia, a deficiency of acid may be partially overcome by hydrochloric acid medication.

2. For digestive purposes hydrochloric acid should always be accompanied by pepsin.

3. In the achylias with diarrhea, acid promises a more noticeable result than in the achylias without diarrhea.

4. When acid produces sourness and stomach irritation its use should not be continued.

5. To avoid acidosis alkalies should be given during the same period, though not at the same time as the acid, the amount required being judged by the effect on the urine reaction.

To avoid the trouble of frequent medication in cases of achylia gastrica I have found it a good plan to have the patient take at the main meal most of the putrefactive protein of the day, such as eggs and flesh foods, the allowance of which is small in these cases, and have the acid and pepsin taken with this meal only. For practical reasons liquid medicine cannot be taken for any length of time after the meal, but doses of 20 or 30 minims of diluted hydrochloric acid and a few grains of pepsin in a full glass of water may be taken with the meal and frequently at half and even one hour later.

THE SOLID HYDROCHLORIC ACID PREPARATIONS. In solid form there are marketed certain drugs purporting to contain hydrochloric acid available for digestive purposes. The best known are *oxyntin*,

a protein compound of hydrochloric acid, and *acidol*, which is chemically betaine hydrochloride. In a careful research under the auspices of the American Medical Association, J. H. Long found that acidol dissociates in an aqueous medium and supplies hydrochloric acid, but that oxyntin holds scarcely enough acid for the digestion of its own protein and cannot therefore supply any for other digestion.

NITROHYDROCHLORIC ACID. Nitrohydrochloric acid has frequently been employed by the older physicians. It is made by mixing hydrochloric and nitric acids, a violent reaction taking place, and the acids being split up to form nitrosyl chlorides and chlorin. There is a slight excess of hydrochloric acid, so that nitrohydrochloric acid of the U. S. Pharmacopœia is a liquid containing free hydrochloric acid, free chlorine and nitrosyl chlorides (Arny). It hardly seems worthy of a place in the materia medica.

BITTERS.[6] In Carlson's tests on a young man in good health, who had an esophageal obstruction and a permanent gastric fistula for feeding purposes, bitters were administered either by stomach fifteen to thirty minutes before meals or by mouth ten minutes before the meal. The patient was in the habit of taking his food by mouth, chewing it and then placing it in the stomach through the fistula. The bitters were the tinctures of gentian, quassia, calumba, humulus and condurango and the elixir of iron, quinin and strychnin. The tests numbered 50 with bitters taken into the mouth, 35 with bitters placed in the stomach and 50 without bitters for control.

When the bitters were taken by mouth they could not be retained long because of the salivation induced and had to be expectorated. Their effect on the appetite of this young man in good health was too slight to be of moment, though it was noted that at the evening boarding house meal, which was never relished, the effect of the bitters was to make an already undesired meal still more undesirable.

When the bitters were placed directly in the stomach small amounts were found to have no influence on the quantity of the psychic secretion or on the acidity or pepsin concentration of the gastric juice. When large amounts were used Carlson's results agreed with those of other observers that their action in the stomach itself was rather to retard than to increase the activity of gastric digestion.

With tests on healthy dogs Carlson further came to the conclusion that bitters acting either in the mouth or in the stomach have no effect on the secretion of the gastric juice.

In another series of experiments Carlson and his colleagues showed that bitters acting in the stomach alone have no appreciable influence on the hunger mechanism as distinguished from appetite,

[6] Carlson, A. J.: The Control of Hunger in Health and Disease, 1916.
Hoppe: 1905, quoted by Moorhead.
Moorhead, L. D.: Jour. Pharm. and Exp. Therap., December, 1915, p. 577.

and that when taken by mouth in the usual way they inhibit gastric tonus and hunger contractions in direct proportion to the intensity and duration of stimulation of the nerve-endings in the mouth. In other words, *in normal people*, so far as they influence the hunger mechanism directly the bitters cause inhibition or depression of hunger.

Arguing from these experiments Carlson takes the ground that the whole value of bitters in medicine is mental and that they are in the same class as an inert but widely advertised patent medicine. He thinks that their continued use depends on two beliefs of the patient, namely, that they will promote appetite, and that anything with a strong and bad taste is strong medicine and therefore good medicine.

On the other hand, Hoppe noted that in a sick dog the use of bitters was followed by an increase in the quantity and acidity of the gastric juice, and Moorhead found that while in normal dogs bitters had no influence on appetite and no influence on secretion or a depression of it; nevertheless, in dogs made cachectic by daily bleedings to produce a chronic anemia they caused a distinct and significant increase in both appetite and secretion. Placed in the stomach without touching the mouth they had no appreciable influence. Barisoff gave tincture of gentian to a dog with the end of the severed esophagus opening outside, so that substances swallowed did not reach the stomach. He followed this with a meal, and in 6 tests without the bitters and 6 tests with found that after the bitters the average amount of gastric juice increased 30 per cent. If he gave the bitters as long as twenty minutes before the meal this effect was not obtained. An excess of bitters checked the secretion.

I myself have noted in many cases of achylia gastrica that bitters have the power to create or increase appetite, though having no effect on the gastric secretion. And I would register my opinion that in many persons with subnormal nutrition, especially in those recovering from an acute illness, bitters have a real value in promoting appetite, and that this action is not dependent on the patient's belief in the efficacy of the drug.

Conclusions. A bitter is useful as an appetizer for those with subnormal nutrition, as in convalescence from acute illness, provided that it is taken not more than five to ten minutes before the time for eating. It acts in achylia gastrica as well as in cases with gastric secretion. In subacidity it promotes the secretion of gastric juice. It should be administered in just sufficient dose to give a strong bitter taste and not in amounts large enough to have a depressant action in the stomach. If the patient is in a state of normal nutrition, but psychically disturbed about eating, it will be useless. If the appetite is already normal the bitter may not only fail to increase appetite but may even lessen it. If the stomach and bowels are deranged bitters may nauseate. The effect on appetite is solely

the local one on the taste buds, therefore it cannot be obtained if the bitters are hidden in capsules or coated pills.

CERIUM:[7] The oxalate, which is the one salt employed, was studied by Baehr and Wessler. They found that it is non-poisonous to dogs even in doses of 50 grams, and that its action is mechanical as a protective to the gastric mucous membrane. Administered in advance it would check the vomiting from a local stomach irritant, such as ipecac, but had no influence on the vomiting from a central emetic, such as apomorphine. They state that the drug is useless in the small doses usually administered and recommend that it be given in doses at least as large as those of the bismuth salts.

BISMUTH.[8] The bismuth salts in common use are the subcarbonate, the subnitrate and the subgallate. The subnitrate is crystalline, and because of this fact probably less bland than the others, which are amorphous. Contrary to the general belief they are all without astringency, that is to say, they do not cause shrinkage of tissues with which they come in contact.

Being basic salts they have the power to take up acid. Theoretically, of *bismuth subnitrate* 1 gram will neutralize 2 c.c. of diluted hydrochloric acid, or the acid of at least 40 c.c. of gastric juice, with the formation of bismuth nitrohydrochloride. But the change takes place very slowly and Böckman has demonstrated that in such acid concentrations as are found in the stomach the subnitrate possesses but little acid neutralizing power. Of *bismuth subcarbonate*, 1 gram will neutralize 4 c.c. of diluted hydrochloric acid or the acid of at least 80 c.c. of gastric juice, with the formation of bismuth chloride. It does not change to bismuth oxychloride as so frequently stated, for this basic salt cannot form in an acid medium. Bismuth subcarbonate changes somewhat more rapidly than the subnitrate, but not rapidly enough to justify attributing any important part of its action to its acid neutralizing power.

In a study of test-meals with the addition of bismuth subcarbonate, and fractionally extracted every fifteen minutes, Crohn reported that 2-gram doses given directly after the meal caused a diminution in acidity without any compensatory increase (as found after alkalies) in the acid secreted. According to a published chart he administered the salt half an hour after the meal, and up to the one and one-half hour period found the acidity slightly higher than in the control. But at one and three-quarters hours he got an acidity of 40 as compared with 70 for the control, and at two and one-quarter hours 50 as compared with 68. There was a slight retardation in the empyting time. In a duplicate experiment with a slightly greater dose the acidity was depressed from 56.8 to 45.2

[7] Baehr, G., and Wessler, H.: Arch. Int. Med., 1908, ii, 517.
[8] Böckman: Arch. Exp. Path. und Pharm., 1916, lxxx, 140.
Böhme, G.: München. med. Wchnschr., 1908, lv, 89.
Crohn, B. B.: AM. JOUR. MED. SC., 1918, clv, 808.

without delay in emptying or any evidence of the secondary rise in acidity which regularly follows the administration during the digestive period of the alkalies and alkaline earths.

Some years ago, in a number of instances, I administered doses of 2 grams of bismuth subnitrate just before or just after the test-breakfast, and though at the end of the hour the stomach contents usually showed a lessened acidity, and also a lessened secretion as determined by the Matthieu-Rémond method, there were a few cases in which the acidity was unchanged. Unfortunately, the protocols and the case records of these experiments were destroyed, so that I am not able to figure a reason why the bismuth should fail in these instances. In every case it was noticed that at the end of the test-breakfast hour the bismuth was uniformly mixed with the extracted stomach contents, and that it had changed from a heavy powder to a flocculent substance that settled slowly with the food. On two occasions I administered to dogs with their food, doses of 2 grams and 8 grams respectively of bismuth subnitrate colored red with carmin, and on removing the stomach and intestines three and seven hours later found the colored bismuth in this same flocculent and comparatively light state, partly mixed with the food residues, but mostly coating very uniformly the whole mucous membrane. In the dog killed at three hours it coated the stomach and small intestines throughout, except the first three or four inches of the duodenum. In the dog killed at seven hours it coated the whole jejunum and ileum. The coating stopped short at the ileocecal valve and there was no macroscopic evidence of bismuth in the colon.

Crohn's results with bismuth subcarbonate and mine with bismuth subnitrate would seem to be of the same nature, and would suggest that the action of either salt is not antacid but rather protective by coating the mucous menbrane. Their power to spread over a large surface of membrane is almost phenomenal. Crohn's work establishes the fact that while the bismuth salts affect the secretions they do not essentially change the motility. By their protective action these bismuth salts would seem to have a value quite equal to that of cerium oxalate in preventing vomiting from local stomach irritants, such as ipecac.

Toxicology. By mouth the bismuth salts are not ordinarily poisonous, though Kohn reported the development of stomatitis and other manifestations of metallic poisoning from doses of 0.3 gm. (5 grains) given four times a day (length of time not stated). But poisoning from the use of a bismuth paste in the treatment of sinuses is not uncommon. One fatality resulted from less than 10 grams of bismuth subnitrate mixed with vaselin. Therefore, it may be conceived as possible that if the bismuth salt given by mouth should be retained on a raw area such as an ulcer, metallic poisoning may occur. As demonstrated by the roentgen rays such retention is unusual, but at our last meeting Jacob Kaufmann mentioned a case

of hematemesis to which Naunyn had given 25 grams of bismuth subnitrate, and in which at the postmortem von Recklinghausen took out of the crater of the ulcer 20 of the 25 grams of bismuth.

The symptoms have the characteristics of poisoning by the heavy metals, viz., stomatitis, salivation, a violet, blue-gray or blackish line on the gums, nausea, vomiting, diarrhea and prostration.

After bismuth subnitrate, but no other bismuth salt, another form of poisoning has occurred, namely, nitrite poisoning, this being due to the formation of nitrous acid. Most of these cases have resulted from the ingestion of large amounts of bismuth subnitrate for roentgen-ray work; but there are a few that have occurred from the medicinal use of the salt. Böhme, for example, reported that after giving an eighteen months marasmic infant several grams by mouth and two days later a similar dose by rectum, the child three hours after the last dose suddenly developed abdominal pain, diarrhea, cyanosis, and dyspnea, and died in half an hour. The blood and pericardial fluid gave tests for nitrous acid, and the blood for methemoglobin. Böhme found that when he mixed bismuth subnitrate with feces, nitrous acid was formed, and that when he placed this mixture in a rabbit's intestine, the urine showed nitrites. In one fatal case E. Meyer demonstrated nitrites in the urine, blood and pericardial fluid.

Silver Nitrate. Before leaving the subject of drugs I wish to put on record a case of argyria that I have just found on my service, with a universal metallic slaty look to the skin, which came on after taking only $\frac{1}{4}$ grain of silver nitrate three times a day for two months.

I also this year had an autopsy on a similar case of argyria, in which the viscera were much discolored with silver deposits. This resulted from the application only once daily of a caustic silver stick to the mouth of a fistula. The period of application I do not know. This may point a moral for men who use silver nitrate in gastro-enterology.

A ROENTGEN RAY SIGN OF PERINEPHRITIC ABSCESS.[1]

By M. H. Fussell, M.D.,

and

H. K. Pancoast, M.D.,

Philadelphia

During the study of Case II in this report a curious fluoroscopic finding was observed which directly led to a diagnsois of perinephritic abscess, and which was confirmed by operation. The same

[1] Read before the Association of American Physicians, Atlantic City, N. J., June 18, 1919.

fluoroscopic sign was noted in Case I, but in this particular case the diagnosis was certain before the fluoroscopic finding was seen, hence no particular attention was paid to it except to note its presence. So far as either of us can discover this roentgen-ray finding has not been previously reported, though, of course, in the mass of literature a notice of it may easily have been overlooked.

Case I.—F. H. W., male, aged thirty years, was admitted to the University Hospital, under the care of Dr. J. B. Carnett, October 2, 1916, with a diagnosis of renal calculus on the left side. The diagnosis was confirmed by roentgen rays and the stones removed by Dr. Carnett. The patient did well until October 10, when he developed fever of a mild type. On October 25 the fever became septic in type and continued until December 13, when a fluoroscopic examination showed fluid at the seat of the operation. This fluid was demonstrated while the patient was standing in the fluoroscope. The shoulders of the patient were grasped and the patient's body moved quickly two or three times from side to side. Watching the fluoroscopic picture showed a distinct wave in the supposed fluid. This observation was made by Dr. Pancoast. He offered the explanation that a collection of fluid was around the kidney, which showed the wave when agitated. The renal region was opened and a huge sac of pus demonstrated within the capsule of the kidney.

No other opportunity was given to discover whether this sign was an accidental one or whether it was common in subdiaphragmatic collections about the kidney on the left side until Case II was seen.

Case II.—A. F., male, aged forty-six years, was seen with Dr. Shelly, of Ambler, Pa., May 14, 1918. The patient had been sick three weeks, was tired and chilly, and had fever of a septic type. He had pain referred to the base of the left lung. A paracentesis had been performed by Dr. Shelly, who had removed 3 or 4 c.c. of clear fluid with a needle from the base of the left chest. When seen by the writer there was pain and tenderness over the region of the left kidney, but nothing else could be detected. A needle was inserted in the left chest, but the tap was dry.

In the history which was obtained there were symptoms indicative of what was thought to be a peptic ulcer; a tentative diagnosis was made of subdiaphragmatic abscess from a perforating ulcer. He was sent to the University Hospital for a roentgen examination, but this was negative, and he returned the same day.

In a week after this his symptoms still continued; he was again sent to the hospital for careful observation. The symptoms were an irregular fever of septic type, with persistent but slight pain over the region of the left kidney. A roentgen-ray examination, with the patient lying on his back, showed the diaphragm to have the normal arch, and nothing particular could be seen. A plate taken, however, showed a beautiful picture of gall-stones, but did not reveal the presence of liquid. Remembering the experience with

Case I, the patient was placed upright in the fluoroscope and the first observation was that the left leaf of the diaphragm was flat and was immobile, and had lost its normal arched position.

The patient's shoulders and body were then moved quickly from side to side, and there was distinctly seen the same wave above the renal region which was observed in Case I. This observation was confirmed by both authors and by several other observers.

In view of these facts an exploration was advised in the left lumbar region, with the belief that all of the symptoms were due to a collection of pus in or around the left kidney.

Dr. A. C. Wood, who performed the operation, hesitated to explore the region because the local physical signs of a collection in that region were so slight, but urged that the gall-stones be removed and the lesser peritoneal cavity be explored. This, of course, was a rational opinion, but because of the curious fluoroscopic sign he was persuaded to open the kidney region. The incision showed the left kidney tightly bound down by its lower half. But surrounding the upper pole an abscess containing approximately 200 to 300 c.c. of pus was found.

The patient made an uninterrupted recovery and was discharged June 25.

On October 30 the patient developed marked symptoms of gall-bladder disease. He was again roentgenographed and the first plates showing gall-stones were confirmed. The gall-bladder was removed and showed thirteen stones. There was no evidence of previous or present collection of pus in the lesser peritoneal cavity. Today the patient is well.

This fluoroscopic sign is reported, because we believe it will be of value in certain obscure cases of fever, with suspicious signs about the left kidney, but which signs are not certain enough to warrant an exploration.

In Case I it will be noted the pus was within the capsule of the kidney; no note was made as to the shape of the diaphragm. In Case II the diaphragm had an entirely normal appearance when the patient was lying down and became flattened when the patient was upright. This phenomenon is not clear to us. We have thought of many explanations, but none seem satisfactory. It will be noted also that the amount of fluid was not large, which makes the sign of value in early cases. This second patient was soon relieved, having been in the hospital only about four weeks after operation.

Of necessity, pus about the right kidney will not be expected to give this sign, as the liver intervenes between the kidney and the diaphragm. So far as we know no such observations of collections of pus between the liver and the diaphragm have been made.

It is confidently hoped that other observers will search for the presence of a wave under the diaphragm in cases of subdiaphragmatic or perinephric abscess when the body is quickly moved from side to side.

EFFECTS OF RESTRICTED (SO-CALLED ULCER) DIETS UPON GASTRIC SECRETION AND MOTILITY.[1]

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AND
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NEW YORK.

(From the Medical Services and the Pathological Laboratory, Mount Sinai Hospital, New York.)

Medical literature offers several studies of the clinical end-results of medical treatment of gastric and duodenal ulcers. The chemism and physiology of the stomach after operation has also been studied. But practically no information can be obtained regarding the direct results upon the stomach of the various forms of medical treatment. Whether clinical improvement during an ulcer cure depends upon a change in the chemistry and motility of the digestive organ remained until recently a matter of speculation rather than a demonstrated fact. The most illuminating articles on this subject are those contributed by W. W. Hamburger,[2] of Chicago. He was able to demonstrate (by radiographic means) during intensive medical treatment the actual healing of ulcers, the disappearance of "niche" phenomena and the restoration of normal peristalsis and motility. While he refers from time to time to changes in the chemistry of the organ as a result of restricted diet, his attention is focussed mainly on the radiographic picture of the healing ulcers.

J. Friedenwald and Baetjer[3] carefully observed radiographically the function of the stomach during medical treatment. Their observations led them to conclude that several weeks, even months, of protracted diet were necessary before the disappearance of signs of abnormal function, such as exaggerated peristalsis, delayed motility, irregularity of contour, etc. The studies of Friedenwald and Baetjer are the first attempt directly to observe the effect of medical treatment on healing ulcers.

It is upon the chemism and the motility of the stomach while undergoing medical treatment that I am attempting to contribute some facts. This paper is based on observations made upon 34 patients. The cases belong in one general group; they were either proved instances of gastric or duodenal ulcer or they were cases suspected of bearing ulcers. In 5 of the patients ulcer was demonstrated by operation at a later date; in 21 of the cases ulcer was the

[1] It is a great pleasure to acknowledge with sincere thanks the kind privileges extended by the attending physicians of the hospital in the course of this study.

[2] Am. Jour. Med. Sc., 1918, clv, 204. [3] Tr. Assn. Am. Phys., 1903, p. 9.

clinical diagnosis, based upon the history, physical findings, chemical data and radiographic evidence. In the remaining 8 subjects the final clinical opinion was that they were suffering from a gastric neurosis or a functional disturbance of the stomach.

The symptoms which these patients presented in common were periodic attacks of heartburn, pain after meals, acid eructations, occasional vomiting and loss of weight. Practically in all these cases hyperacidity was chemically demonstrable, hypersecretion was frequently present and delayed emptying of the digestive organ was a prominent factor.

Since intra-abdominal diagnosis at its very best is conceded to be inaccurate and open to error, it is better in this study to consider the effects of the diet upon the chemistry of a diseased stomach *per se* rather than upon the ulcer when and if present. In this study no light is thrown upon the pathological changes that an ulcer undergoes during medical treatment. Only the immediate effects of the dietary restriction are studied. The observations extended, as a rule, over from two to five weeks in each case; the remote effects of medical treatment are not considered.

PROCEDURE. The routine examination of these patients upon admission consisted of a careful history and physical examination, extraction of fasting gastric contents, Ewald test breakfast and other chemical tests, stool examinations for occult blood and finally a thorough radiographic examination. A fractional test-meal to establish the type of curve was also performed. After the collection of all data the patient was placed upon a restricted diet for a period of from two to four or more weeks. During the period of observation, fractional test-meals were taken every few days. The type of the acid curve, its maximum height, its duration, the presence of hypersecretion, the emptying time, etc., were carefully noted for any changes that could be interpreted as due to the form of treatment being instituted. Clinical notes were made from time to time so as to ascertain a possible parallel between improvement in subjective symptoms and a change for the better in the disturbed chemism of the organ. The fractional test-meal was chosen as the best laboratory method for the demonstration of the phases of gastric digestion. By this method, so intimately associated with the name of Rehfuss, the height and duration of the acid secretion can be computed and plotted, evidence of pathological hypersecretion becomes manifest and the emptying time of the organ accurately estimated for a given and constant test-meal (oatmeal gruel in this study).[4]

BASIC PRINCIPLES OF SO-CALLED ULCER DIETS. There are certain general characteristics which are common to all forms of so-called ulcer diet. These are:

[4] Crohn and Reiss: AM. JOUR. MED. SC., 1917, cliv, 857.

1. Administration of highly nutritious foods in small quantities, frequently repeated.

2. Neutralization of the free acid of the digesting stomach.

This is accomplished by administering high proteid foods, mainly milk, with the addition of eggs and later of cereals. Antacid salts are commonly employed to assist the neutralizing action of the foods.

An improvement in the motility of the stomach is sought in cases in which emptying time is delayed. In the series studied, patients were subjected either to a Lenhartz diet carried out without modification or to a diet similar to the one advocated by Sippy.[5] In the diet as we administered it, milk and cream in small doses (2 or 3 ounces) were given hourly during the day for the first three days; cereals were then added twice daily. At the end of a week two eggs a day were added and puréed vegetables were gradually introduced. All forms of meat were withheld until the third week. Antacids in small quantities were given between feedings; bismuth was a constant component of these powders. Occasionally gastric lavage for food stasis was employed, though this was fortunately rarely indicated.

Before proceeding to discuss the general effect of such a diet upon the gastric chemism, let us study the individual chemical reaction which results upon the introduction into the stomach of these various foods. As a control one should keep in mind the normal curve of secretion, while employing oatmeal gruel as a test-meal or the usual Ewald test breakfast. Chart I demonstrates the reaction of a patient with a normal curve to a test-meal consisting of 240 c.c. of milk. One notes immediately the fact that milk causes a high total acidity (up to 128 c.c. $\frac{N}{10}$ sodium hydrate per 100 c.c.); that the height of the acidity is maintained for three or four hours; that free acid is present in larger quantities than usually met with in cereal or bread test breakfasts, and that the stomach takes considerably longer to empty itself. The acid-binding qualities of milk are apparent in only the first half-hour; thereafter to the end of digestion free acid is liberally present.

Compare this with the exaggerated effects of a combination of milk and eggs (Chart II). The total acid curve mounts still higher, reaching a maximum of 146 per cent.; free acid becomes evident after one and a half hours and is present in strong concentration during the remainder of the digesting cycle. Emptying time is, as a result, prolonged, even allowing for the large amount of test-meal given. A free hypersecretion of concentrated acid persists after the disappearance of the last traces of food.

The behavior of a cupful (280 c.c.) of clear bouillon, as recommended in the von Leube diet, is similarly interesting (Chart III).

[5] Jour. Am. Med. Assn., 1915, lxiv, 1625.

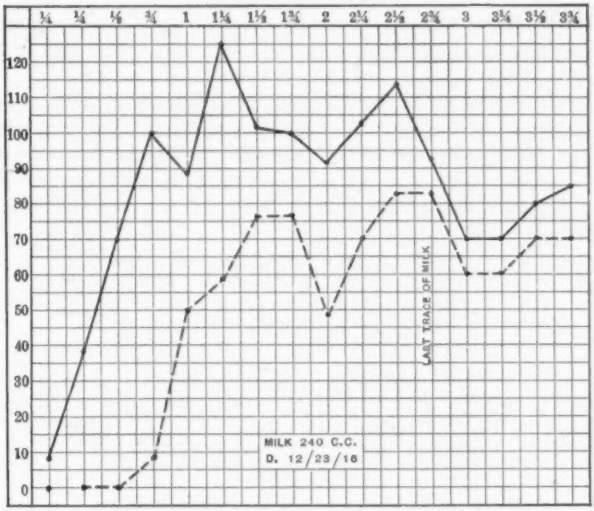

CHART I

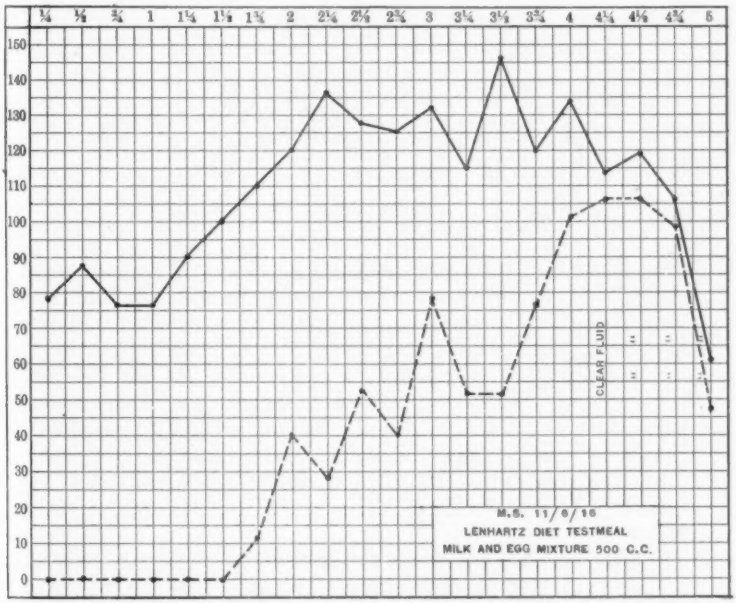

CHART II

No considerable binding of acid is at any time demonstrable. A high acidity, both free and total, quickly takes place and is maintained for two hours; thereafter the stomach is empty.

The conclusions to be drawn are: Milk is a strong acid stimulant and is only slowly emptied through the pylorus. The combination of milk and egg is a powerful stimulant to gastric secretion, causing a hyperacidity and hypersecretion, with prolongation of the emptying time. Bouillon fails to bind acid and is a mild digestive stimulant.

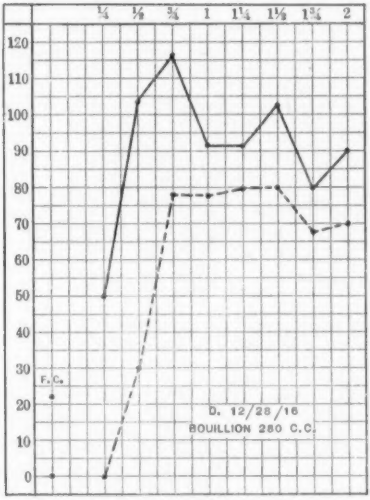

CHART III

The justification for the frequent repetition of food in small quantities is seen in Chart IV. Here we observe the effect upon the secreting organ of three ounces of milk repeated hourly. While the total acidity remains moderately high (average 80 per cent.) very little free acid is allowed to accumulate. As the free acid curve tends to rise toward the conclusion of each fifteen-minute period it meets the new portion of milk imbibed and is immediately neutralized. Since peptolytic digestion occurs only in the presence of free acid, it is apparent that in so far as actual splitting of the compound proteid molecule is concerned this stomach is really inactive.

If to this hourly administration of milk we add an alternating small dose of antacid salts (bismuth and bicarbonate or magnesia and bicarbonate in 5-grain doses of each as advocated by Sippy[6]), we are enabled to note (Chart V) that free acid entirely disappears and

that even the total acidity is strongly controlled, averaging only 43 per cent. Peptolysis is absent throughout.

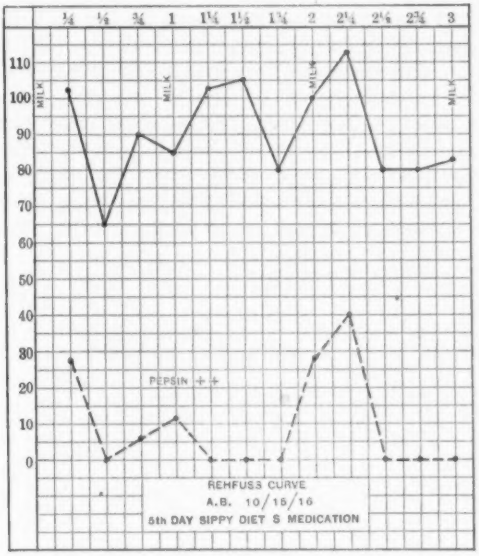

CHART IV

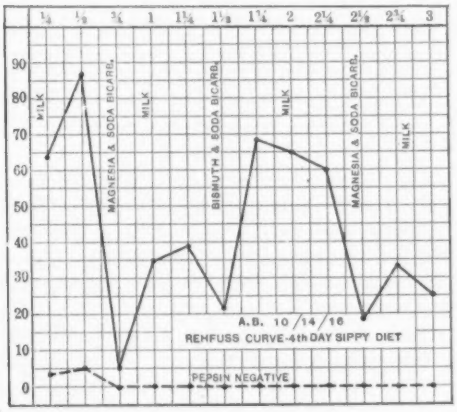

CHART V

If the reduction of total acidity and the complete neutralization or combining of free acid were the aims of this form of medical

treatment, then surely this plan of alternate milk and antacids fills all the requirements and offers the stomach the optimum conditions of anacidity for the cure of an ulcer.

However, of late much doubt has been thrown upon the hypothesis that ulcer of the stomach is due to the corrosive action of gastric juice. This theory really gained headway before the realization by the older clinicians of the fact that duodenal ulcer outnumbers in frequency gastric ulcers. The charted curve of acidity in the duodenum during digestion regularly fails to show the presence of any free acid, nor is the total acidity at any time high (Chart VI). The similarity between this chart and the preceding one is striking. Our approved methods of medical treatment aim to accomplish in

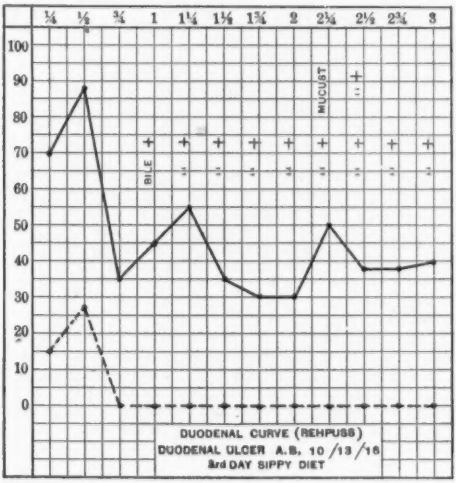

CHART VI

the stomach the very conditions of combined or neutralized acidity which are regularly and normally present in the so-called juxtopyloric portion of the stomach or duodenum. Yet under these very highly desirable and optimum conditions of anacidity duodenal ulcers appear and grow.

A closer study of the entire subject tends only to raise more doubts as to the *modus operandi* of cure of ulcers by medical treatment. The causal relationship between the hydrochloric acid and ulcer has not been proved, nor are we able unquestionably to accept the hypothesis that the cure of ulcer depends on the neutralization of the free acid of the stomach.

However, clinically, the beneficial results of medical treatment cannot be denied or gainsaid; it behooves us therefore to proceed to

study the effects of days and weeks of the administration of such a regimen on the gastric secretion.

Effect of Medical Treatment on Gastric Acidity. Of the 34 cases which constitute the basis of this study 11 cases had an isosecretory or hyposecretory curve and 24 a hypersecretory curve of acidity (Rehfuss[6]). Let us assume that a beneficial effect of the medical treatment would be the diminution of an excessive hyperchlorhydria and a return to a normal or hyposecretory type of curve. In the series observed, medical treatment succeeded in causing a definite lowering of the acid curve in 6 of the 11 cases, with iso- or hyposecretory curves; 5 of the 11 were unaffected or unchanged. Of the cases with marked hyperacidity, numbering 23 in all, only 7 showed a lowering of the acid curve; in the remaining 16 the curve remained high in spite of persistent and rigid dieting and rest in bed.

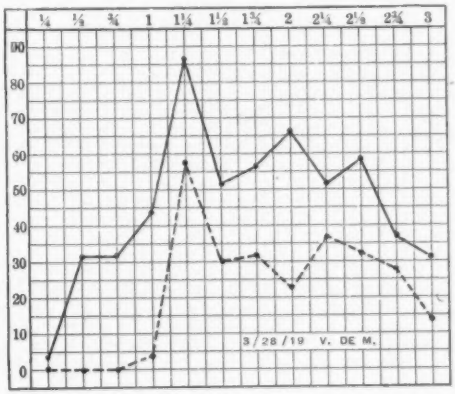

Chart VII

The lowering of the acid curve was often very marked, much more so in cases of hyperacidity than in those with normal or subacidity. Chart VII is the curve of a case of functional hyperacidity (operative findings negative) before the institution of treatment. Chart VIII the same case on the tenth day of a Lenhartz diet. The lowering of activity, diminution of hypersecretion and improvement in motility are marked.

Cases with normal curve of secretion, though suffering with symptoms of heartburn and belching, often show a similarly striking reduction of acidity to a subnormal or hyposecretory status.

Chart IX is the curve before treatment of a case of probable duodenal ulcer, with symptoms three years in duration; radiographically a persistent duodenal irregularity and stasis were visible.

[6] Jour. Am. Med. Assn., 1914, lxiii, 11.

Chart X is the curve of the same patient on the fourth day of a Lenhartz treatment, Chart XI on the seventh day and Chart XII

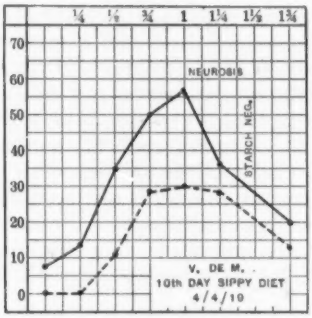

CHART VIII

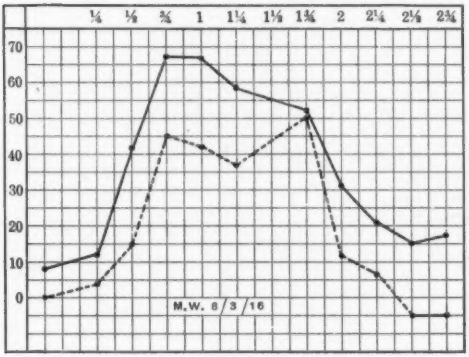

CHART IX

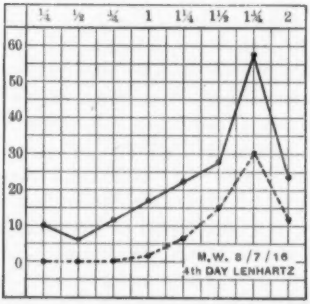

CHART X

on the twelfth day. The progressive lowering of acidity was accompanied by gradual improvement of subjective symptoms and disappearance of epigastric tenderness on pressure. This case, however, differs from the majority of the cases showing improvement, in that the reduction of acidity takes place as early as the fourth day of treatment. In most of the patients the chemical improvement was not demonstrable before the fifth to the seventh day. In more favorable cases the reduction of acidity began about the end of the first week of restricted diet and was maintained to the end of the period of observation. All of these cases but one were accompanied by marked relief from subjective clinical symptoms.

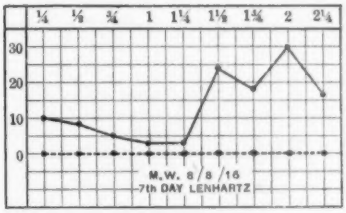

CHART XI

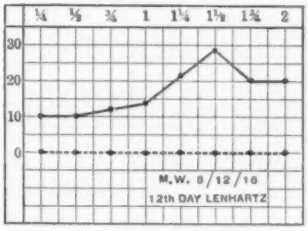

CHART XII

Of the 21 cases in which no reduction of acidity could be demonstrated little need be said; their curves resisted, many of them, even protracted restriction of diet, often meat-free for weeks. In spite of this more than half of these cases showed clinical improvement some of them markedly so.

The introduction of meat on the tenth day of the Lenhartz diet or the fourteenth day of the modified Sippy diet often converted a case which was tending toward diminished acidity into one with persistent hyperacidity. The following case is an illustration of this kind. The patient was one who had been suffering for seven months with symptoms of duodenal ulcer. A large indurated ulcer of the duodenum was in fact demonstrated at operation several months later. Chart XIII is the curve upon admission to the hospital (service of Dr. Manges).

Chart XIV the same on the fourth day of Lenhartz diet.

Chart XV the same on the sixth day of Lenhartz diet.

Chart XVI the same on the tenth day of Lenhartz diet, scraped beef having been given the patient for the first time on the previous day. The marked increase in acidity is noteworthy.

Chart XVII the same patient on the twelfth day of Lenhartz diet, meat having been removed from his diet. A slight improvement is noted.

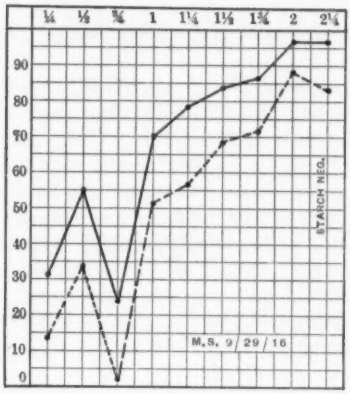

CHART XIII

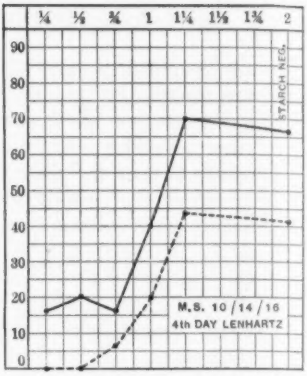

CHART XIV

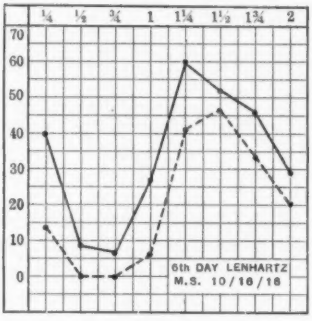

CHART XV

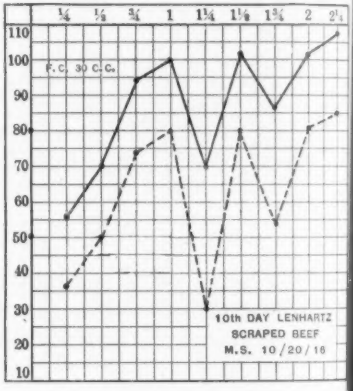

CHART XVI

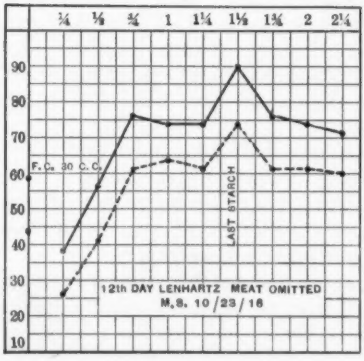

CHART XVII

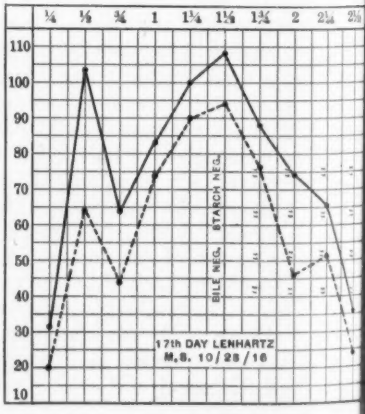

CHART XVIII

Chart XVIII is the curve on the seventeenth day of diet, still meat-free. Note the persistence of hyperacidity.

Repeated fractional tests of this patient were made up to the twenty-eighth day of the diet. (See Charts XIX and XX.) The hyperacidity hereafter failed to be reduced. The patient was discharged from the hospital free of subjective symptoms. Within a few weeks he returned with recurrence of his symptoms and was subsequently referred for surgical interference.

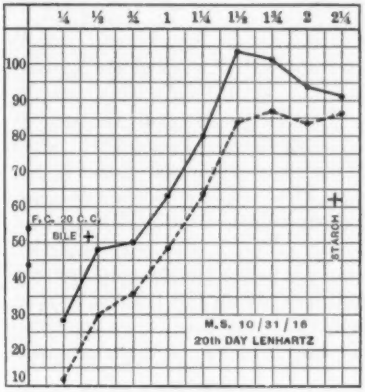

CHART XIX

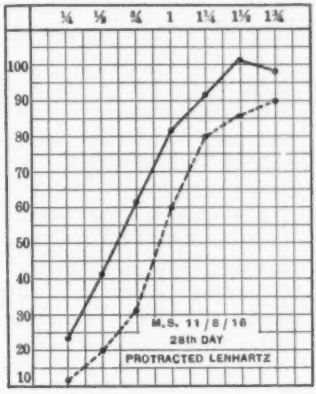

CHART XX

A vital question must occur to one's mind at this point. Is the reduction of hyperacidity which takes place during medical dietary treatment paralleled by clinical improvement, and conversely is a resistant hyperacid curve accompanied by persistent gastric symptoms?

Taking the cases as a whole 13 were chemically improved, 21 were not, a net chemical improvement of only 38.3 per cent. Yet clinically 25 of the 34 cases were discharged from the hospital free of symptoms, a percentage of 73.5 per cent., not quite as high as those presented by Lenhartz or von Leube, but still high. Of the 13 favorable cases in which the acid curve was reduced and the hyperacidity obliterated, 12 left the hospital symptom-free.

On the other hand, of the 21 cases with a persistent high acid curve in spite of treatment, 13, or 62 per cent., were markedly clinically improved. The remaining 38 per cent. (8 cases) left the hospital with the same curve as on admission, and clinically unimproved by their treatment.

A certain parallelism between chemical and clinical results is obvious.

TABLE I.

Acid curve, reduced, 13 (38 per cent.).
Clinically improved, 12 (92 per cent.).
Clinically not improved, 1.
High acid curve, persistent, 21 (62 per cent.).
Clinically improved, **13** (**62** per cent.).
Clinically not improved, 8 (38 per cent.).

The figures in heavy type are the interesting group, namely, those in which the curve remained acid-fast, and yet the patients left the hospital free of symptoms.

EFFECTS OF RESTRICTED DIET AND REST IN BED UPON GASTRIC HYPERSECRETION. The fractional test-meal is an ideal medium for the demonstration of hypersecretion. As the successive samples are removed from the stomach at quarter-hour intervals the proportion of food or cereal to the digestive fluid becomes smaller. With normal motility the last portion of the gruel disappears at two hours. It is at this time that hypersecretion when present becomes evident, for from this point one removes every fifteen minutes a sample of secretory fluid unadulterated by food. This is the pure secretion of gastric tubules; it is usually profuse so that large amounts can be removed, and it continues sometimes for several periods or even hours after the food has passed the pylorus. In exaggerated instances as much as 30 c.c. of pure acid fluid can be removed every five minutes.

The exact clinical significance of alimentary hypersecretion (we shall omit from present discussion continuous hypersecretion) has yet to be determined. Strauss,[7] Zweig[8] and others who noted the phenomenon described it as a pathological factor and ascribed its presence to the existence of an organic lesion of some part of the alimentary tract. Gastric or duodenal ulcer, chronic appendicitis or reflex irritation of gall-stones were and are all held responsible for the stimulation of this excessive fluid. But opinion is not uniform on the significance of its presence, and we need only quote Rehfuss,[9] who in a recent article spoke of hypersecretion as being of no pathological importance and of its presence in several normal controls.

The period in the cycle of digestion in which hypersecretion is most evident is the period following the evacuation of the food. The titer of this hypersecretory fluid is usually high in acid, averaging from 60 to 80 per cent.; practically all of it is free acid; only a very small percentage is present as combined acid and practically none as acid salts. It is at this period that the pains of ulcer are often most marked; this remains true whether we ascribe the pains

[7] Deutsch. Arch. klin. Med., 1895, lvi, 120.
[8] Arch. Verdauungs., 1907, xiii, 143.
[9] Jour. Am. Med. Assn., 1918, lxxi, 1535.

to the direct action of the excess of free acid upon the ulcer or the stomach wall or whether we attribute the pains to the exaggerated peristaltic waves or hunger contractions which become evident during this part of the digestive cycle.

Whatever the significance, hypersecretion is a common phenomenon in gastric and duodenal ulcer; it was present twenty times in this series of 34 cases, appearing toward the end of the period of food digestion as a postdigestive or alimentary hypersecretion.

We are interested in knowing what effect, if any, medical treatment, consisting of a marked restriction in food and rest in bed, has upon this factor. A close association is noted between hypersecretion and hyperacidity; 16 of the 20 instances of hypersecretion were in cases with gastric hyperacidity. In 9 of the 20 cases, where

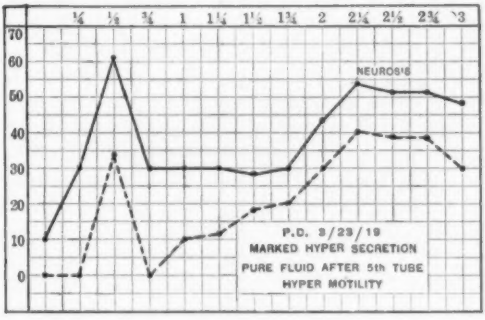

CHART XXI

present, hypersecretion was markedly improved or caused to disappear by medical treatment, a percentage of 45 per cent. In the other 11 cases, or 55 per cent., no effect was noted. The beneficial results of treatment were often very marked in this respect. Thus, for instance, Chart XXI is the curve of a case of gastric neurosis with hypersecretion, this curve being taken upon admission to the hospital, service of Dr. E. Libman. Chart XXII is the same case after six days of modified Sippy diet. Note that the character of the curve has changed; the acidity is somewhat higher but the hypersecretion is less marked, and the stomach empties itself in one and three quarter hours. Chart XXIII is the curve on the twelfth day of the diet. The curve is quite normal, the observation on the chart at the end of two hours being "scant secretion;" emptying time is normal. Many well-marked examples of the effect of medical treatment in causing the disappearance of hypersecretion could be demonstrated in the cases of this series. In fact, this is one of the most striking effects of medical treatment when a good result is present.

Much disappointment was felt in that the beneficial effect was not accomplished in a greater percentage of the cases. Eleven cases, or 55 per cent., were in nowise modified by either the restricted diet, the use of antacids or the physical and psychical rest accompanying the stay in the hospital. It is hardly possible to explain the failure in this not inconsiderable percentage of the cases.

Does improvement in hypersecretion accompany a reduction in hyperacidity, or, in other words, are both factors effected in the same manner by the medical treatment? A reference to Table II is instructive.

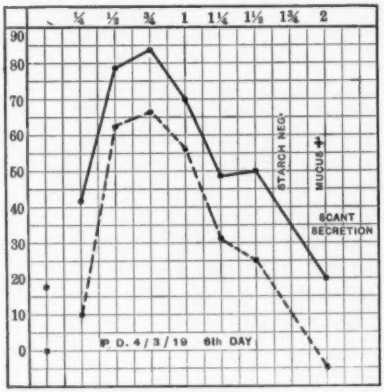

CHART XXII

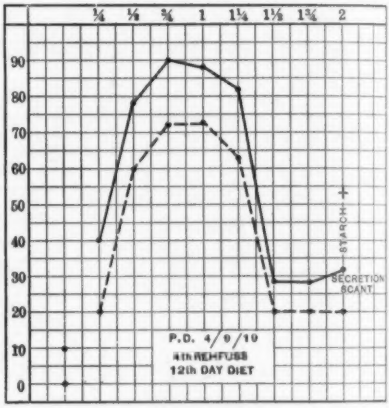

CHART XXIII

TABLE II.

Hyperacidity reduced; hypersecretion improved; clinical result: good, 6 cases; poor, 1 case.

Hyperacidity not reduced; hypersecretion not improved; clinical result: good, 8 cases; poor, 3 cases.

Hyperacidity not reduced; hypersecretion improved; clinical result: good, 2 cases. Total, 20 cases.

It is thus seen that in all but 2 cases, the last two in the table, both factors were identically influenced, either both being beneficially influenced or neither one affected for the better. The frequent coexistence of these two factors, and their similarity of behavior under treatment, suggests a close association between them.

As for the clinical results of treatment the same inconsistency is naturally seen in this group as in those in which only the effect on hyperacidity was considered. While in 11 cases, or 55 per cent., the treatment failed to affect the hypersecretion, yet 16 of the 20

cases, or 80 per cent., were discharged from the hospital clinically much improved and actually free of symptoms.

EFFECT OF MEDICAL TREATMENT ON GASTRIC MOTILITY. What is the result of our medical efforts upon delayed emptying of the stomach and persistent food residue?

Before proceeding directly to a critical review of the cases let us consider for a moment, as a preliminary, the question, "Is the fractional test-meal a good medium by which to judge the motility of the stomach?" There has been much discussion as to the relative merits of the roentgenological method for demonstrating delayed motility, and, on the other hand, of chemical methods for demonstrating postponed emptying. Both methods have undoubted value, and either method in the hands of a competent technician and observer, is beyond question, a reliable index of motility.

The fractional test-meal by allowing observations at such short intervals as a quarter of an hour seems to have the advantage over both other methods, these latter being limited to a single observation at the termination of a stated interval. With the fractional method one can state within a few minutes just when the last remnant of food has passed the pylorus. In every instance in which a six-hour residue was reported by roentgen-ray methods a chemical delayed motility was also evident with the Rehfuss method. On the other hand innumerable instances are met with in which slighter grades of delayed emptying are evident by this chemical method, which evade entirely the roentgenologist.

Using 500 c.c. of thick oatmeal gruel as a test breakfast, normal motility with the fractional method may be regarded as one and three quarters to two hours; in cases with moderate degrees of atony up to two and a quarter hours.

In this series of 34 cases of ulcer, or ulcer suspects, there were 13 instances of delayed motility, using the fraction test as a criterion. The time of emptying varied from two and a quarter hours to a maximum time of three and a half to four hours. It is in this field that the optimum effect of medical treatment was obvious.

The following two charts illustrate the improvement in motility which resulted in a case in which the diagnosis of penetrating ulcer of the lesser curvature was radiographically demonstrated. Chart XXIV is the curve taken upon admission to the hospital (service of Dr. E. Libman). Note that after three hours the iodin test for starch (oatmeal gruel) was still ++. After twenty-six days of treatment (Chart XXV) shows emptying time reduced to one and a half hours. This result is striking.

Or, another case, one of probable gastric ulcer; symptoms one and a half years in duration; periodic remitting attacks of heartburn and eructations and loss of weight. Chart XXVI is the curve on admission (service of Dr. E. Libman). The note on the chart reads "three and a quarter hours p. c., starch ++." Chart XXVII is the

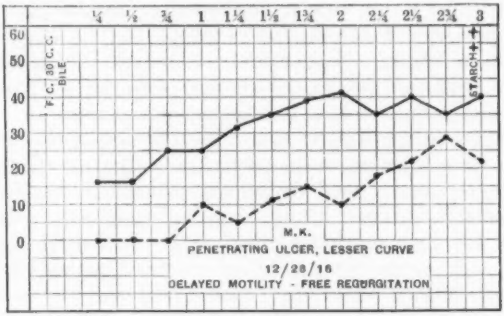

CHART XXIV

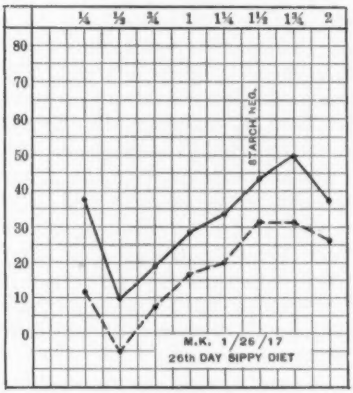

CHART XXV

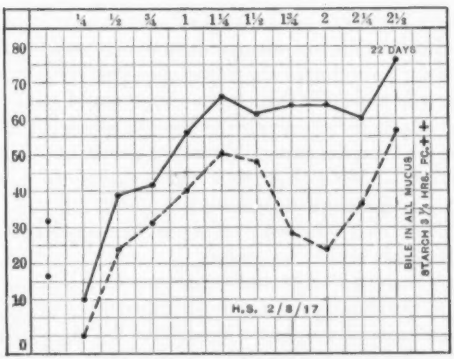

CHART XXVI

curve of the same case after six days of strict dieting; after two and a quarter hours the stomach has already evacuated the last traces of starch.

The preceding 2 cases are undoubtedly examples of delayed motility due to pylorospasm, for it is hardly conceivable that a real organic stenosis would have resolved in so short a period as six days, as obtained in the second of these 2 cases.

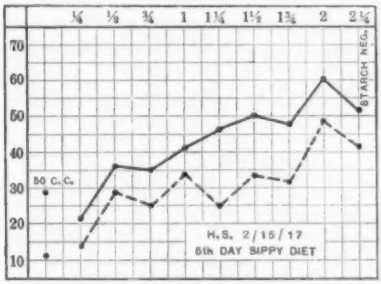

CHART XXVII

The following charts demonstrate the results of medical treatment in a case of organic stenosis due to pyloric ulcer. The patient, a man, aged fifty-four years, had been under my observation for about

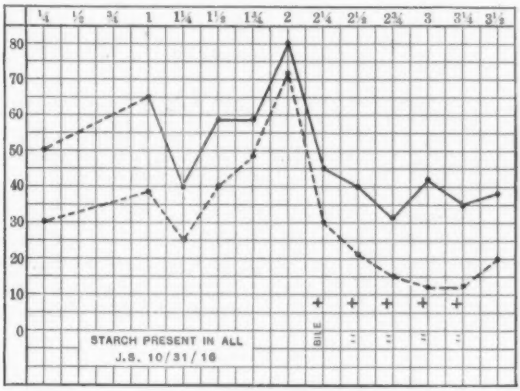

CHART XXVIII

two years. He had residual vomiting, periodic pain and loss of weight; his Ewald test breakfast showed high acidity, sarcinæ, yeast and marked food stasis. Repeated radiographic examinations failed to show a defect or suspicion of carcinoma, though confirming the delay in evacuation. Chart XXVIII is the acid curve upon

admission (service of Dr. E. Libman). At the end of three and a half hours starch was still present in all the specimens withdrawn. Chart XXIX is the curve on the ninth day of treatment. After three hours starch is still present in all tubes. Chart XXX is the curve on the fifteenth day of modified Sippy diet. Starch is present as a trace after two and three quarter hours, and is absent after three hours. It is also noted that the acid curve now falls to normal when the stomach becomes empty.

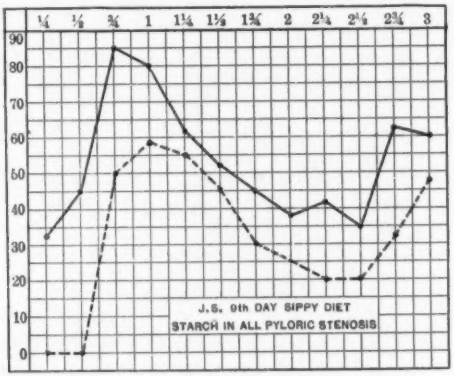

CHART XXIX

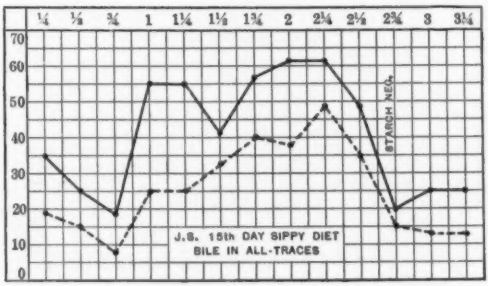

CHART XXX

In all but two of the cases of the series emptying time was definitely, in many of them markedly, shortened, a proportion of 85.4 per cent. Still more striking is the fact that clinical improvement as noted ran quite parallel with the reported improvement in motility. All of the 11 cases in which improved motility was accomplished were discharged free of symptoms, while the 2 cases in which the delay in motility resisted our efforts were discharged unrelieved of subjective symptoms.

A reduction of acidity did not always accompany an improvement in the motility. Thus of the 11 cases with improved emptying time, in only 3 was hyperacidity reduced, while in the remaining 5 the high acid curve persisted. In spite of the persistent acidity all of these cases were discharged free of symptoms.

Hypersecretion was noted 6 times in association with delayed emptying. In 4 of these 6 instances it was not relieved by the treatment; in these cases, though, the hypersecretion persisted, the pyloric stenosis or pylorospasm was relieved and the patient was discharged free of symptoms.

The following is a tabulation of the results of motility test which followed treatment and the day upon which the test was taken:

TABLE III.

	Motility before treatment.	After treatment.
Case 12	2¼ hours	1¼ hours (12th day)
16	3 "	2¼ " (6th day)
17	2¾ "	*2¼ " (12th day)
21	3¼ "	3 " (9th day)
		2¾ " (15th day)
23	3½ "	2¾ " (7th day)
		1½ " (10th day)
		1¾ " (12th day)
24	3 "	2½ " (3d day)
		2½ " (8th day)
27	2½ "	2½ " (6th day)
28	2½ "	*2¾ " (3d day)
		2¾ " (12th day)
30	2½ "	1¾ " (10th day)
34	4 "	1½ " (26th day)

* No improvement.

Discussion. Having studied in detail the effect of restricted diet and rest in bed upon each of three factors which show deviation from the normal, let us try to evaluate the relative importance of the change which takes place in each of them. Let us attempt to estimate the relationship between clinical relief from symptoms (cure?) and physiological or chemical benefit.

Does medical treatment reduce the hyperacidity of ulcer, and if so, is this relief responsible for the clinical improvement?

Does restricted diet cause the disappearance of hypersecretion, and if it does, is this the factor that relieves the symptoms?

Finally, can delayed motility in the presence of ulcer be relieved by the feeding of small quantities of food often repeated? And if so, is this the factor that brings about apparent cure of symptoms? We will discuss these factors individually and collectively, recapitulating the findings in the body of the paper.

Medical treatment resulted in a net reduction of acidity in 13 out of a series of 34 cases (38 per cent.). If we wish to consider only those cases with definite hyperchlorhydria, omitting all cases with iso- or hyposecretory curves, the percentage of net lowering of acidity

is still lower (30.3 per cent.). Of these 13 cases chemically benefited 12, or 92 per cent., were discharged free of symptoms. Loose reasoning might lead one to see a relationship of cause and effect in these figures. But if we analyze those cases in which treatment failed to invoke chemical relief, and these comprise the larger proportion, we find, despite this fact, clinical relief in 13, or 62 per cent., of them. In other words, of 25 cases discharged from the hospital free of symptoms and apparently well, 13, nearly one-half, retained the same height and type of acidity as on admission. If clinical cure depended upon relief from hyperacidity then the optimum result should be in this class of cases. Almost 80 per cent. of the cases with hyperchlorhydria left the hospital clinically relieved, yet only 30.3 per cent. of these showed chemical relief from the excessive acid production.

We can draw two inferences from these figures: (1) Only a small percentage of ulcer cases react to medical treatment by showing a reduction of acid produced during digestion (38 per cent.); (2) clinical improvement can take place independently of whether the hyperacidity is relieved or whether the case remains acid-fast.

As regards hypersecretion a similar conclusion is soon arrived at. Twenty cases in the series showed hypersecretion; in 9 cases, or 45 per cent., medical treatment caused the disappearance of this abnormal factor, in the other 11, or 55 per cent. of the cases, medical treatment failed to alter the hypersecretion. Yet 80 per cent. of these cases left the hospital apparently well. Exactly 50 per cent. of the clinically cured cases still retained hypersecretion upon discharge from the hospital, and yet subjectively the pyrosis, heartburn and pain had disappeared.

From these figures we can again draw two conclusions: (1) Medical treatment, consisting of restricted diet and rest in bed, causes the cessation of hypersecretion in 45 per cent. of the cases, a fair proportion; (2) clinical improvement takes place as often in cases with persistent hypersecretion as in those relieved of their excessive flow of gastric juice, and is apparently not dependent upon it.

Finally, we shall discuss the relationship between improved gastric motility and clinical relief. There were 13 cases of delayed motility; in 11, or 85.4 per cent., medical treatment succeeded in alleviating this symptom and reducing the emptying time to normal. All of these 11 cases were in addition freed of subjective complaints. Two cases resisted treatment (motility unimproved), and they were discharged clinically unrelieved.

There are no instances of clinical cure that could be solely attributed to reduced acid secretion when delayed motility was present as a complicating factor. Unless relief is had from the pylorospasm we fail to note the disappearance of subjective symptoms. By stating that relief of pylorospasm results in clinical cure and is probably the cause for amelioration of symptoms we have only answered

part of the question. Most of the cases in this series were not complicated by delayed motility; they were cases with hyperacidity and hypersecretion but normal motility. We have tended throughout this study to discredit the idea that clinical relief is built upon a reduction of the hyperacidity or hypersecretion and can and does take place independent of chemical change.

Then to what change in the physiology or pathology of the stomach can one attribute the relief from symptoms in cases not complicated by pylorospasm? No data in this study throws any light on this question. The answer must be sought and will probably be found in the radiographic studies of Ginsberg, Tumpausky and Hamburger,[10] Carlson,[11] Hardt[12] and others.

These authors have demonstrated the close relationship between subjective pain and exaggerated peristalsis or hunger contractions. It is quite likely that restricted diet and bed rest have a quieting influence upon gastric contractions, diminishing the amplitude and violence of these contractions. Reduction of acidity and secretion may or may not accompany the reduced tonus of the stomach.

The present study has demonstrated that in a fair proportion of the cases medical treatment caused reduction of hyperacidity and of hypersecretion. To what can be attributed the failure to effect this change in a far larger percentage? The answer probably lies in the fact that the marked restriction of food intake is not maintained for a long enough period. Almost all schedules of "ulcer diet" increase the number and amounts of food rapidly, particularly during the second week. In fact, Lenhartz already introduces meat on the tenth day. It is a common observation that hospital patients complain bitterly of being starved in the early days of dieting, yet it is just at this period that they report the disappearance of their annoying subjective symptoms. The end of the second week, which usually marks the period of increased alimentation, is a common date for reappearance of symptoms of pain and heartburn. It has further been shown that it takes up to the sixth to the tenth day for the acid secretion to show beneficial result, as evidenced in a lowering of the curve. The earliest effect of the marked food restriction is probably diminished tonus and contractions and increased rest to the stomach walls. The later effect is a fall of acidity and secretion. The full beneficial result, particularly on the hydrochloric acid production, is probably defeated by a too early return to a more liberal diet. The introduction of meat during the second or third week is harmful; meat-free diet should be continued for weeks or even months.

It is probable, too, that a diet based in its earlier stages on milk alone, rather than on milk and eggs as in the Lenhartz diet is to be

[10] Jour. Am. Med. Assn., 1916, lxvii, 990.
[11] Am. Jour. Physiol., 1917, xlv, 81.
[12] Jour. Am. Med. Assn., 1918, lxx, 837.

preferred. The amount of secretion called forth in the digestion of a milk-egg diet is far greater and the emptying time is much longer for a milk-egg mixture than for a milk meal, or certainly for a cereal meal. Personally, I would favor rather a greater liberality and earlier introduction of cereals and more restraint in the use of eggs.

It has been demonstrated in a previous paper by the author[13] that antacids should be used often and in small doses, lest they in themselves increase or stimulate the acid cells to production. Nor can the influence of the psychical factor be overlooked. Mental contentment during a course of treatment is essential. A noisy hospital ward; the bad example of a bed-neighbor who is a neurotic and constantly complaining of the food, the treatment and his symptoms; mental disturbance over economic conditions at home, are all influences that tend to cause persistence of secretory and motor abnormalities and deprive the patient of the full benefit of his rest in bed and dietary cure. This principle applies as well to the ulcer cases as it more evidently does to the cases of functional secretory disturbances or neurosis. A patient who is unhappy during his treatment is unlikely to get well.

One cannot overlook the physical difficulties of treating many cases by "ulcer diet" in a busy hospital ward. The war intensified these difficulties many times by creating a shortage of nurses. It is not an easy matter for a limited number of ward nurses to serve milk every hour, give antacid medication on the alternating half-hours and look after the general wants of the patients in addition. Cereal which has been delayed in transit and becomes cold is tasteless and to many patients disagreeable to eat. I fear that many of the failures to obtain better results are due to the physical inability of even the best hospital staff to live up to the details and the schedule of these time and attention-consuming dietary regimens.

Segregation of cases and special nursing facilities would solve many of these difficulties. This probably explains why the results in private practice are far better and more permanent than those in the hospital public service.

Cases that fail to show clinical and chemical improvement are of two kinds: those with advanced indurated ulcers which are resistant to treatment and those with marked neurosis. The first class can be reduced in number by more persistent and more protracted treatment. The second group requires the expert care of a neurologist, often of a psychanalysist. Mistakes in diagnosis undoubtedly form a third group of not inconsiderable proportion. The beneficial effects of medical treatment are seen in those cases of hyperacidity, hypersecretion and pylorospasm accompanying latent cholelithiasis or chronic appendicitis, as well as in ulcer cases or functional

[1] Crohn: Jour. Am. Med. Assn., 1918, clv, 801.

secretory disturbances. This remark applies to immediate results rather than to permanent benefits.

It is to be regretted that the cases in this series could not be observed for a sufficiently long period to determine the durability of the result and to determine whether a relation existed between improved physiological function and permanent cure or relief.

There is a large field for research still open along these lines. Much remains to be learned regarding the physiology and pathology of the stomach during and after medical treatment. It is only by close study and observation that we will learn to account for our failures and learn to recognize the factors that contribute to the clinical cure of these patients.

CLINICAL EXPERIENCE WITH SAHLI'S SPHYGMOBOLOMETER.[1]

By Nathaniel Bowditch Potter, M.D.,

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When this study was first begun nearly ten years ago it was with the purpose of applying a method of studying the circulatory efficiency of chronic diseases in measurable units, and so, of estimating the effect of drugs, of exercise, of rest, of food and of other extramedicinal measures, in order to prescribe any or all of them sufficiently accurately to promote the most rapid recovery, to continue the greatest efficiency and to avoid overloading the circulation.

Up to then no functional tests of the efficiency of the circulation, even as satisfactory as the modern functional tests of renal elimination, had been devised, especially for chronic invalids with damaged hearts, vessels and kidneys. The method of *Sphygmobolometry*, which the Swiss clinician founded upon the dynamics rather than upon the statics of the circulation, certainly promised much; and the later simplified and more accurate method of *Volume bolometry*, even more.

I purposely limited my two previous papers[2] of this series,

[1] From Memorial Laboratory and Clinic, Cottage Hospital, Santa Barbara, California.

[2] Potter, N. B.: Sahli's Pocket Sphygmobolometer; Demonstrated at a meeting of the Medical Section of the New York Academy of Medicine, November 19, 1912. Potter, N. B.: Sahli's Volume Sphygmobolometer; A Recent Improvement over the older Pressure Sphygmobolometer; Am. Jour. Med. Sc., October, 1918, No. 4, clvi.

practically to little more than a description of the instruments, awaiting a clinical contribution long expected from the Berne Clinic. Its place, however, has been usurped by highly technical articles which have from time to time appeared in various German journals of internal medicine, largely theoretical disputes between the erudite Director and one of his former pupils, Christen. Most modern clinicians, surfeited by carefully studied and prepared methods of exactitude, and instruments of precision, have acquired the habit of following lines of least resistance, avoiding polemic discussions, and largely utilizing only the exact, and the, so to speak, ready-made. This natural and mentally lazy tendency, and the incidence of the long war have unfortunately prevented, at most clinics, both here and abroad, the recognition as well as the application of this new conception and method of studying the circulation.

A THIRD INSTRUMENT. The writer's modification of the Volume Bolometer. After several years' experience with both of these

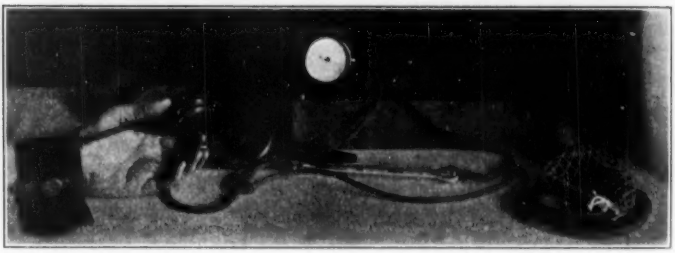


FIG. 1

instruments, the writer became convinced that a more compact and portable instrument, and one less liable to break in transportation could be made; in other words, one so conveniently constructed as to require no setting up and taking down each time it was used at a different place, and quite as serviceable for house-to-house practice as such American Sphygmomanometers as the Tycos and Sanborn instruments. The writer has, therefore, devised and had constructed, with the aid of one of his assistants, Dr. R. R. Newell, the simple modification exhibited in Fig. 1. It requires no further description than this illustration to make its advantages apparent. It enables the observer to take the blood-pressure immediately before or after he makes the Sphygmobolometer estimation, with the same spring manometer. It is so combined as to be very compact, portable and non-breakable, and can be applied, taken off, repacked in a box $10 \times 4\frac{1}{2} \times 2\frac{1}{2}$ inches and slipped into the observer's bag with the greatest ease and despatch. In this respect the writer feels

he owes a distinct apology to the distinguished inventor, knowing the latter's well founded objections to the substitution of a spring for a mercury manometer. If any reasonable demand for such a combined instrument occurs, Dr. Sanborn has been kind enough to offer to supply it.

A few paragraphs will suffice to dispose of the pressure bolometer, and perhaps this can best be done by quoting from one of Professor Sahli's personal communications. From our own point of view it is only necessary to inform the reader that we also had entirely substituted the latter for the former instrument, that some of the suggestions he so kindly gave us we find very helpful for the volume bolometer, as we did for the pressure instrument. We have made something more than a thousand observations with the pressure and two thousand with the volume bolometer, from which the data, tables and charts presented below have been collected. In the following charts and tables we have indicated observations which were made by the original pressure instrument; also those obtained with use of the volume bolometer by our group of workers in New York and at the Memorial Laboratory and Clinic, Santa Barbara, California. My reasons for this are, that although in the main our observations have proved uniform with both instruments and with both groups of workers, there has been, almost from the start, great difficulty and delay in obtaining duplicate instruments, fresh supply of rubber tubing, pelottes, etc., and the substitutes and crude repairs have been relatively so unsatisfactory, especially since the war, that some discrepancy in our figures has unavoidably occurred.

We may here quote from Sahli's personal communication:

"In regard to the comparison between the estimation of the 'Pulse Work' with Volume and Pressure instruments which you have again requested, I can add nothing to what I have already published. This proves that the two methods reveal approximately equivalent values for the pulse work; that the principle for both is correct and that if we employ sufficient care in the optimal adjustment of the cuff, and with the pressure instrument this detail is often tedious and difficult, we can obtain values for 'Pulse Work' which are clinically useful. Since these values in the figures published do not deviate much, one from the other, and since the optimal pressure with the proper application of the cuff does not usually vary markedly in the two methods, the pulse volume (considering the optimal pressures as equivalent) may be readily reckoned in pressure bolometry from the values for the 'pulse work.' 'Pulse Work' is equal to the 'Pulse Volume' times 'Optimal Pressure' times sp. gr. of hg. Perhaps, for the purpose of this communication, this last (sp. gr. hg.) has no significance, so that I have disregarded it.

"As far as your own estimated figures are concerned (a series of observations made upon some of my patients with the estimations and equations worked out in detail which I submitted to Prof. Sahli for criticism) your method of reckoning is correct. I have taken the pains to go over them all very carefully, and have found only quite unessential variations, probably due to the technique of your figuring."

For the reader who is interested the later bibliography upon the subject of Sphygmobolometry is appended below. There are, however, in addition to the Professor's own communication, several papers of considerable interest. The first,[3] from the Berne Clinic itself, concerns the combination of Sphygmobolometry and Jacquet's Sphygmography, for the details of which the reader is referred to the original article. The second,[4] from Naegeli's Clinic at Tübingen, in which a number of observations are reported. Many of them are made with the original pressure instrument, chiefly upon normal individuals, upon a series of long-distance runners before and after a test run, and upon oarsmen before and after a race. The majority showed a sharp rise in the work of the pulse at the end of the exercise, which he considers a normal response. A few showed no effect, or a diminution in the work, which he regards as evidence of a weakened circulatory reaction, and which he explains in one case by a drinking bout the night before, and in another by the remains of an old myocardial lesion.

The author, Hartman, tested four students before and after a drinking bout, with the uniform result of an increase in pulse-rate and drop in the pulse work. Again, he made numerous tests upon a few students after an excessive consumption of coffee, tea and nicotin, as well as many times after a moderately excessive ingestion of alcohol, practically always resulting in a considerable increase in the bolometric values. He concedes the difficulty of formulating a definitely normal value, but shows in four individuals how little the pulse work varies in one and the same individual, over a period of from five to six months. Upon the basis of measurements on fifty students, he formulates the normal between 6 and 14 g.cm. In older and stronger individuals the upper normal limit may reach as high as 15, and in younger males and in females, fall as low as 4½. One of his experiments with twenty students shows how wide a variation may exist in the values obtained from the same individual, without any pathologic reason therefor. During the course of the spring season two measurements show approximately constant values, but the third time upon an extremely relaxing and

[3] Sahli: Ueber die Verwendung moderner Sphygmographen, speziell des Jaquet'schen, zu sphygmobolometrischen Untersuchungen. Die Sphygmobolographie eine klinische methode, Corr.-Bl. f. Schw. Aerzte, 1911, Nr. 16.

[4] Hartman, Carl: Untersuchungen mit dem neuen Sphygmobolometer nach Sahli, Deutsch. Arch. f. klin. Med., 1915, Bd. 117.

oppressingly hot summer evening, sixteen out of the twenty showed an increase of from 1 to 2.5 g.cm. Most of those examined, including myself, very few of whom were physicians, felt the excessive filling of the arm veins. Upon a few pathological individuals before, during and after the use of digitalis, caffein, etc., his records, charts and the description of his work show careful, accurate observation, and are closely in accord with our own results.

He concludes as follows:

1. In perfectly healthy individuals the bolometer values vary excessively—from 6 to 13 or 14 g.cm.

2. The values in a single individual, however, remain remarkably constant over months.

3. Diurnal, physiological conditions, however, lead to not inconsiderable variations, which exhibit themselves characteristically with the bolometer conditions, even when no deviation can be shown by any other method. Therefore the analysis of Sphygmobolometric measurements, make our knowledge of physiologic, as well as pathologic, alterations considerably more profound than delicate.

4. The study of a continuous curve upon one individual, charted out over a considerable period of time, is especially valuable.

5. Physiological efforts, such as occur in sports, like long-distance running and rowing, will, if the test calls forth a moderate effort, produce a moderate increase in the bolometric value; a greater effort will produce a corresponding rise, and as the strength wanes, so too, does the bolometric value decrease.

6. The consumption of alcohol, tea, or nicotin exhibits similar alterations.

7. In the study of the capacity of the cardiovascular apparatus in pathological cases one obtains valuable conclusions from the bolometer.

8. Digitalis therapy gives successful results in the elevation of the bolometric values. When such decrease, so too, does the therapeutic effect of the drug.

9. Support in prognostic conclusions is afforded by this method, when all other methods fail.

Another important article is from the Clinic of the master himself.[5] Regarding this article Sahli wrote me as follows:

"It was not until Dr. Dubois had almost completed his thesis upon pressure bolometry that volume bolometry originated, so he was unable to utilize it. It was soon evident that most of his values were lower than the corresponding volume bolometric values."

"Unable to oversee his work minutely I cannot be sure that each estimation was made with an optimal application of the cuff; nevertheless his clinical observations are quite serviceable if limited to the comparison of one and the same individual at different times, since

[5] Dubois: Sphygmobolometrische Untersuchungen bei Gesunden und Kranken, Deutsch. Arch. f. klin. Med., 1916, Bd. 120.

the chief defect depends upon the anatomical configuration of the wrist-joint region, and so in the estimations upon the same person the figures vary but slightly. Although he had estimated a large series of normal values, at my insistence they were not included in his publication because my assistant, da Cunha, will establish these for volume bolometry alone and later on will publish them. I do not want to cause confusion by presenting two sets of normal values."

The article of da Cunha[6] to which Sahli refers, gives us normal values for the volume of the pulse and for the pulse work, which, despite the inherent difficulties of the method and its interpretation, are of no little utility in the estimation of pathologic cases. Da Cunha's summary follows:

Statistics for normal males, age sixteen to forty-nine years:

Radial pulse volume: Maximum, 0.15 c.cm.; minimum, 0.05 c.cm.; average, 0.09 c.cm.

Radial pulse work: Maximum, 17.14 g.cm.; minimum, 6.12 g.cm.; average, 11.27 g.cm.

Minute's volume of radial pulse: Maximum, 11.2 c.cm.; minimum, 3.0 c.cm.; average, 6.81 c.cm.

Statistics for normal females, age sixteen to forty-nine years:

Radial pulse volume: Maximum, 0.11 c.cm.; minimum, 0.04 c.cm.; average, 0.07 c.cm.

Radial pulse work: Maximum, 17.95 g.cm.; minimum, 5.98 g.cm.; average, 10.19 g.cm.

Minute's volume: Maximum, 8.8 c.cm.; minimum, 2.4 c.cm.; average, 5.56 c.cm.

After a seven o'clock breakfast, taken in bed, the pulse-rate increases, but there is little variation in the volume and work of the individual pulse. Half an hour after a large midday meal the volume and work of the individual pulse, rise, whereas the pulse-rate remains stationary. Two hours after the midday meal the pulse volume resumes its original value. The pulse work likewise decreases, but not with the same regularity. It may return to its original value or it may fall slightly above or below it. The rate of the pulse is now lower than before the consumption of food.

Charts 13 and 14 illustrate my own observations on normal or approximately normal subjects before and after the noon meal.

On changing from a lying to a sitting posture there is an acceleration of the pulse, but in both pulse volume and pulse work there is a decrease so great that, despite the increase in pulse-rate, there is a distinct fall in the minute's volume and the minute's work.

My observations in regard to posture are illustrated by Chart 6.

Da Cunha's article shows that his work was done in the usual

[6] da Cunha, D. Jose: Beiträge zur Beurteilung der Resultate der Sahli'schen Volumbolometrie nach Untersuchungen bei Gesunden, Corr.-Blatt f. Schweizer Aerzte, 1917, Nr. 46.

accurate fashion of the Berne Clinic. Most of his observations are quite in accord with our own. His illustrations are unusually simple, clear, and striking. This paper should be consulted by anybody planning to utilize the instrument and the method.

On account of the war, four of the more recent publications[7] have been, and still are, inaccessible to the reader on this side of the water. However, Reinhart's very recent article[8] reveals much of what is most essential. Reinhart regrets the extreme paucity of the literature.

Brösamlen entirely discards the method because of the influence exerted upon the values he obtained by varying vasomotor conditions. He denies that any conclusions of permanent value in regard to the cardiac-systole can thus be obtained. In his last communication Sahli replied to the above criticism, pointing out the incomplete and incorrect protocols upon which Brösamlen's conclusions were based; also his entire neglect of the pulse-rate, and failure to report the pulse volume in addition to the work. Individual variations of the caliber of the radial artery, as induced by the effect of heat and cold upon the arm, may of course have been responsible for considerable fluctuation in the pulse volume, and so too, may general vasomotor influences. Sahli believes, however, that, taking all factors, such as pulse-rate, into consideration, dependable values for the measure of the volume of the circulation can be obtained, unless there are gross vasomotor or anatomical abnormalities of the radial artery.

Reinhart, using the new sphygmovolumeter with great care as to application of the cuff, endeavored to determine, by simple experiments in which the volume of the heart-beat could be considered positive, whether a demonstrable increase or diminution of the systole would also be manifested in an increase or diminution of the sphygmovolumeter volume. Working with large and small hearts, on the theory that, aside from anomalies such as mitral insufficiency, a larger heart must be associated with a larger heart-beat volume, the author obtained results which conformed in every respect with the roentgen-ray findings. In 130 examinations made with the sphygmovolumeter on 30 normal individuals and 25 patients with valvular lesions, this author demonstrated the fact that the volume of the pulse diminishes as the patient changes from horizontal to

[7] Brösamlen: Die Bedeutung der Pulsuntersuchung f. die Bemessung des Herzschlagvolumens, Deutsch. Arch. f. klin. Med., 1916, Bd. 119. Dubois: Sphygmobolometrische Untersuchungen bei Gesunden und Kranken, Deutsch. Arch. f. klin. Med., 1916, Bd. 120. Müller, O., und Brösamlen: Ueber die Eignung der Sphygmobolometrie resp. Sphygmovolumetrie zur Bemessung der Systolengrösse resp. des Minutenvolumes, Deutsch. Arch. f. klin. Med., 1917, Bd. 124. Sahli, H.: Ueber die richtige Beurteilung der Volumbolometer und die Art ihrer Klinischen Verwendung zugleich Erwiderung auf den Aufsatz von Dr. Brösamlen, Deutsch. Arch. f. klin. Med., 1917, Bd. 122.

[8] Reinhart, A.: Ueber die Eignung der Sphygmovolumetrie zur Bemessung der Systolengrösse, Deutsch. Arch. f. klin. Med., 1918, vol. cxxvii.

the upright position, corresponding directly with the diminished size of the heart in the upright position. This decrease averaged 20 per cent. to 30 per cent., but in individual cases amounted to 45 per cent. to 50 per cent. in special patients. In these experiments, as the volume decreases the pulse-frequency rises, thereby partly, but not entirely, compensating in minute's volume for the reduction in size of the single pulse. Corresponding with the diminution of the volume, the maximal pressure also drops as a rule 10 to 15 mm. of mercury.

In a series of experiments with the Valsalva test, Reinhart demonstrated a diminution of the sphygmovolumetric pulse volume conforming with the decrease of heart-beat volume demonstrated by the roentgen ray. This diminution of the pulse volume points to a diminution of the heart-beat volume, and, *vice versa*, a diminution of the heart-beat volume points to a diminution of the pulse volume.

In a third series of experiments, it was demonstrated that fluctuations in the pulse volume occur under forcible inspiration and expiration. In pulsus paradoxus and respiratory arrhythmia the smaller systoles at the beginning of the inspiration were associated with smaller pulse volumes. Sixty cases without respiratory arrhythmia showed, with few exceptions, a decrease in the pulse volume at the beginning of inspiration, corresponding to the theoretical decrease in the systole on inspiration.

In his fourth series of experiments the author found that in changes of frequency of cardiac contractions, induced by stimulation or paralysis of the vagus nerve, by means of pressure and of atropin respectively, the high-frequency contractions were accompanied by smaller pulse volumes than were the low-frequency contractions.

Finally, it was shown from pathological cases that pulse volume is dependent on heart-beat volume; as in cases of compensatory disturbances with a small systole and in pulmonary edema with failure of the left ventricle, where a distinct diminution is noted in the volume of the pulse, pulse volume again increasing under improvement of the circulation.

Reinhart, then, in his carefully executed experiments, establishes that the pulse volume as measured by sphygmovolumetry is directly dependent on the size of the systole; hence the pulse volume registered by the sphygmovolumeter affords a method for determining the size of the systole. These experiments seem positively to refute the violent attack made upon sphygmovolumetry by O. Müller and Brösamlen.

What is this dynamic measurement? Is it of clinical value, sufficient to justify the amount of training, patience and time essential to its employment? It was not until some years after *Sphygmomanometry* had been demonstrated to be an essential addition to any physical examination, that it was proved beyond peradventure

that even an expert could not estimate blood-pressure with any degree of accuracy by ordinary finger palpation of the artery alone, although this had formerly been supposed possible. For centuries every physician has been palpating the pulse in order to be able to determine by the pressure of his finger an approximate value of *pulse volume* and indirectly, although generally unwittingly, a rough measure of *pulse work*. Without discussing the value of such dynamic pulse conceptions, or even whether they do actually furnish determinations of the same relative value as for the heart itself, it may be stated positively here that none of us who have been working with these instruments have the slightest doubt that the ordinary finger palpation of the pulse is incapable of furnishing even a skilled observer much if any more dependable results in this dynamic measurement than, unaided by an instrument of precision, he is able to obtain of blood-pressure with its static measurement. If we can prove, therefore, that these dynamic measurements are of clinical value, either in diagnosis, prognosis, or treatment; that they can be reasonably accurately determined by Sahli's latest instrument, the so-called *Volume bolometer;* that the essential skill and experience for its use can be obtained by any competent clinician or laboratory technician within a brief period; and that the procedure requires but a moderate amount of time for each estimation; we shall then have definitely demonstrated that the fecund Swiss clinician has added another and a most valuable method for accurately studying the circulation, and one from an entirely new viewpoint. The older method *Sphygmobolometry* or *Pressure bolometry* has been entirely discarded by its originator at his Clinic at Berne and permanently supplanted by *Volume bolometry*. Our observations, however, with the earlier method may be utilized in a tabular and statistical form to prove that even with this inferior, much less accurate, and much more time-consuming method, quite dependable results were obtained by my assistants after but a few weeks' training and experience.[9]

With the aforesaid purpose in view, we have, therefore, made no special or definite effort to establish a table of normals, based upon either decade, sex, size or weight; or to more than point out such gross differences in both *pulse work* and *pulse volume* as are well exhibited by such cases as an emaciated, weakened, starving diabetic, well-compensated aortic insufficiency, essential high blood-pressure, or an enormously hypertrophied heart from long-standing chronic nephritis. Such differences will be frequently noted in the

[9] I acknowledge with much appreciation and thanks the devotion, patience and industry of Drs. Bradbury, Ordway, Brownlee, Ramurez and others who made these observations from which these tables and statistics were collected. Before their results were fairly uniform and trustworthy, each one of them required from three to eight weeks' practice, depending largely upon their previous experience with instruments of precision. Of course their observations were not utilized until they had developed this degree of skill.

figures below. After several years' experience I believe that this new method of studying the circulation will prove to be of essentially more value in comparing the daily figures furnished by a single case, or of the effects of various methods of treatment, medicinal or extra-medicinal in some one individual than in helping us to diagnose the disease in question or even to compare one patient with another by a single bolometric determination upon each. In the first place a number of determinations would always be necessary in order to

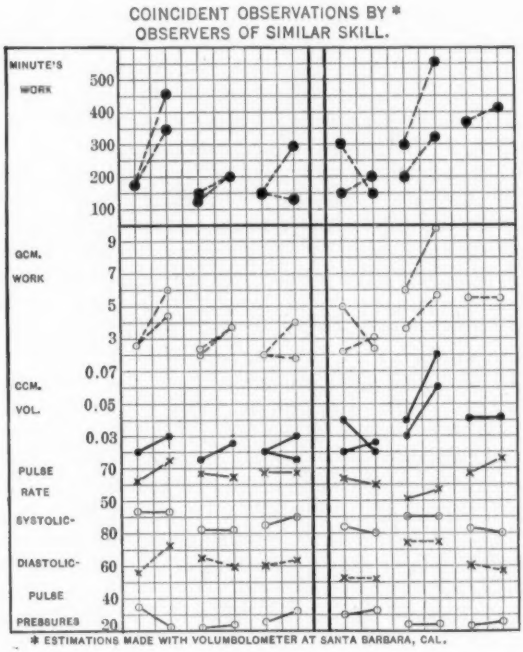


CHART 1

arrive at an approximately uniform figure for this or that individual patient's normal. In the second place each patient's normal radius is relatively wide, especially so as compared with the border limits, and is influenced by many temporary, even momentary, emotional and other unavoidable causes. However, after what may be called the normal variations for an individual are once determined the effect of various causes when measured in *gram-centimeters of* WORK, or better still of MINUTE WORK, should prove of considerable clinical value.

ACCURACY. Chart 1 shows the results of coincident estimations on opposite wrists of the same individual by two observers of reasonably similar skill and experience. As will be seen in most instances, the agreement is striking. Where such wide discrepancies result as the last reading on Case 1, and the first reading on Case 2, it is generally because of the differences of the size and position of the radial artery, perhaps most often the latter; for in the many emaciated diabetic patients upon whom most of these tests were

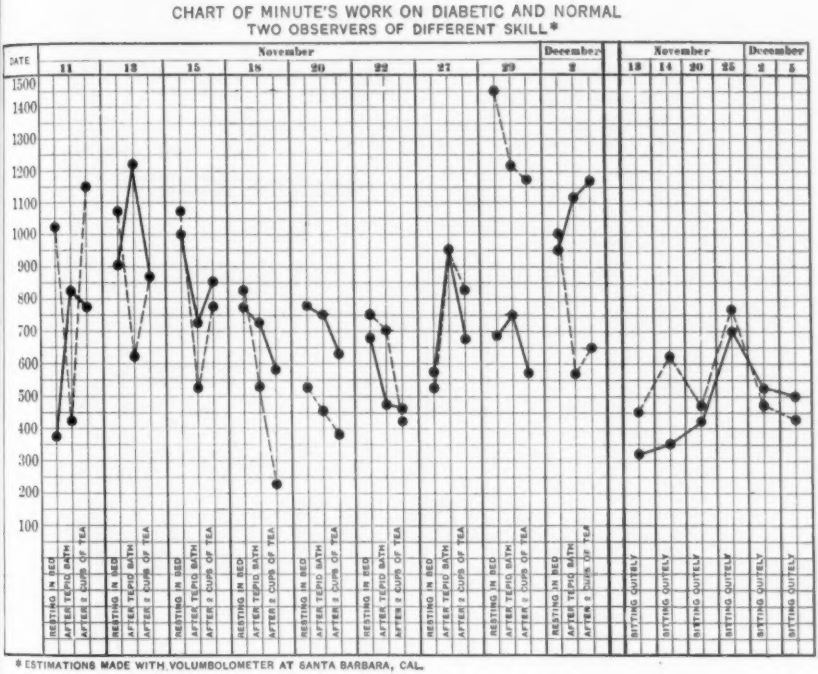
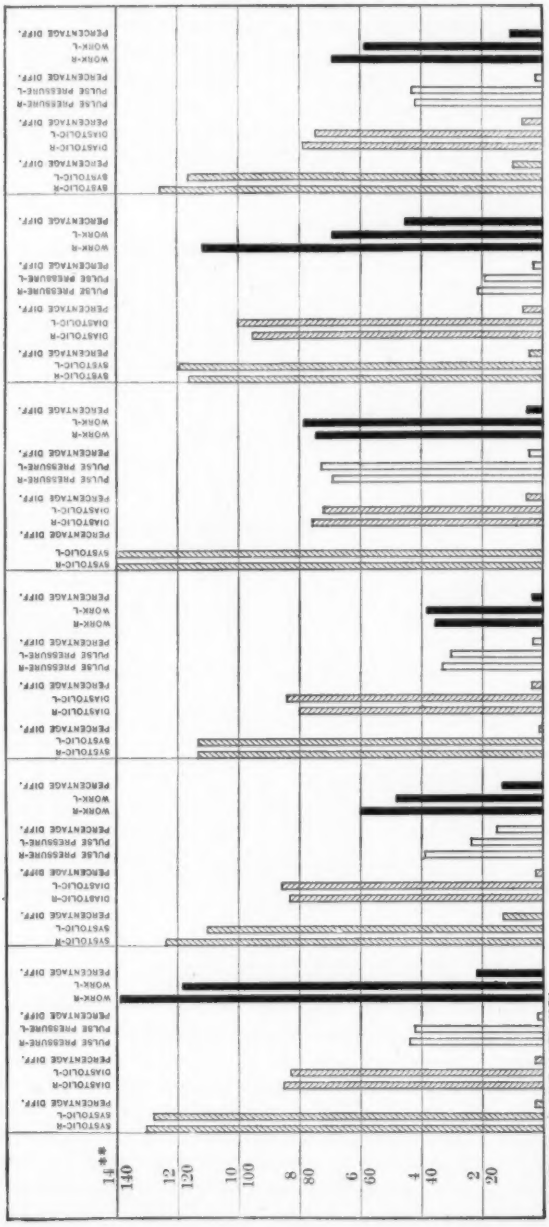


CHART 2

made, the difficulty of adjusting the wristlet properly is almost insurmountable, requiring infinite time, patience and frequent repetitions.

Chart 2 shows the variation between similar observations made by observers of markedly different skill and experience.

Chart 3 compares graphically the percentage of variations in the two wrists when the observations were made by the same worker under as nearly as possible identical conditions, the one immediately after the other, utilizing systolic, diastolic and pulse-pressures and



* ESTIMATIONS MADE IN NEW YORK.
** NUMBERS ABOVE LINE REFER TO OGM. WORK, THOSE BELOW LINE REFER TO BLOOD PRESSURE.

CHART 3

work. Although the blood-pressure is much more in conformity, yet the difference is not striking.

Thus it may be concluded that there is scarcely less of accuracy or variation in this modern method *Volume bolometry* than in *Sphygmomanometry*.

Time Required to Become Expert. Prof. Sahli states ten minutes, but this time varies so greatly with the individual technician that it is difficult to obtain definite figures. My experience, however, with the many assistants who have so devotedly aided me in this study has led me to conclude that, like most other painstaking methods of precision with relatively delicate instruments, the whole affair is largely a matter of temperament, considerably a matter of training in similar methods, and no little dependent on the great quality of patience. From twenty-five to one hundred estimations usually fit a competent, well-trained technician to make dependable estimations.

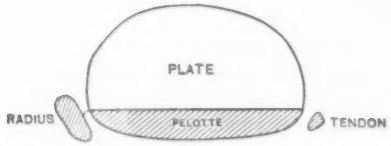


Fig. 2

Time Expended Upon Each Determination. Each determination requires, according to the speed of the technician, and the type of patient, especially the position of his radial artery, upholstery of fat about the tendons, and configuration of his wrist, from two to three times that required to perform a systolic and diastolic blood-pressure determination by the usual auscultatory method with the Tycos or Sanborn instrument.

Applicability, Convenience and Annoyance to the Patient. Delirious patients with pneumonia, thrashing about continually, render such estimations extremely difficult, or impossible; but the ordinary quiet delirium of typhoid fever, or pneumonia, scarcely increased the difficulty of its application. The essential importance of a placid temperament in the observed as well as in the observer is self-evident. In Charts 13, 14, 15 and 16 any reader can readily select which of the observed individuals belong to this enviable category and which have an emotional, excitable, unstable nervous system. Variations in *Minute Work* represented by more than 100 per cent. have been observed to follow such slight nervous influences as the interruption of a telephone message. After all, it is wise to keep in mind that one essential feature of the greatest importance in the correct interpretation of incongruous results should first be attributed to the configuration of the wrist and to the

varying application of the cuff. In this respect, Prof. Sahli wrote me the following helpful suggestions:

"Great variations in the configuration of the tissues at the wrists of different individuals is responsible for one of the most telling difficulties in each application of the cuff for a proper optimal pressure. In one person the application is extremely easy, in another much patience and time are required on account of the way the plate is supported on one side by the styloid process of the radius and on the other by the tendon of the flexor carpi ulnaris, bridging over to a certain extent the pelotte in an excavation of the plate, thus:

"One frequently applies the plate *farther up* the arm because in bony and tendinous individuals it is impossible to succeed at the usual point of application, whereas, in addition to the separation of bone and tendon higher up, the better upholstered soft parts are also of assistance. Another help is sometimes afforded by *revolving the plate* along its long axis.

"The *throttled manometer* which I formerly employed to avoid a loss of energy, proved superfluous and I discarded it. It too may be responsible for mistakes in pressure values because *sometimes with the higher pressures it does not register correct values.*

"The *glass connections*, too, must be of the same very small calibre. All these affect the multiplication factor, ϕ, which only applies to the caliber, the length of the conducting tubes and the air content of the system above mentioned. Though very impractical, leaden tubes would be preferable to rubber tubes in pressure bolometry.

"In pressure bolometry spontaneous relaxation of the cuff must be carefully avoided, for despite its very good application the vigorous pulsating force exerted, may gradually cause it to yield and even to become definitely distended. This change is much less liable to occur in volume bolometry because of the much less decided variations in pressure. As a result of such yielding there may arise materially incorrect (too small) pressure bolometric values.

"Certain possible errors may occur even in the reading. As you have noted yourself, they depend upon the effect of the variations in the respiration and of Traube's waves (periodic vascular contractions) continually dislocating the index and altering the size of the excursions. Hence, when the excursions are small much practice is needed to read them accurately, especially in pressure bolometry. So, too, the endpoint of the excursions is difficult to determine in the frequently lightning-like rapidity of the pulsations, because the retinal impressions are so transitory that one scarcely appreciates the index endpoint which persists near the latter so very brief an instant as to produce scarcely any color appreciation. This difficulty is all the more accentuated because the extremity of the index is not a straight cross line, but a sort of swollen meniscus

scarcely visible, as a result of the rapidity of the motion. The *lower meniscus* less bowed than the upper is, therefore, more easily read and gives frequently higher readings than the upper. The same difficulty occurs in both instruments, but is more significant in pressure bolometry where the absolute size of index is less. Since

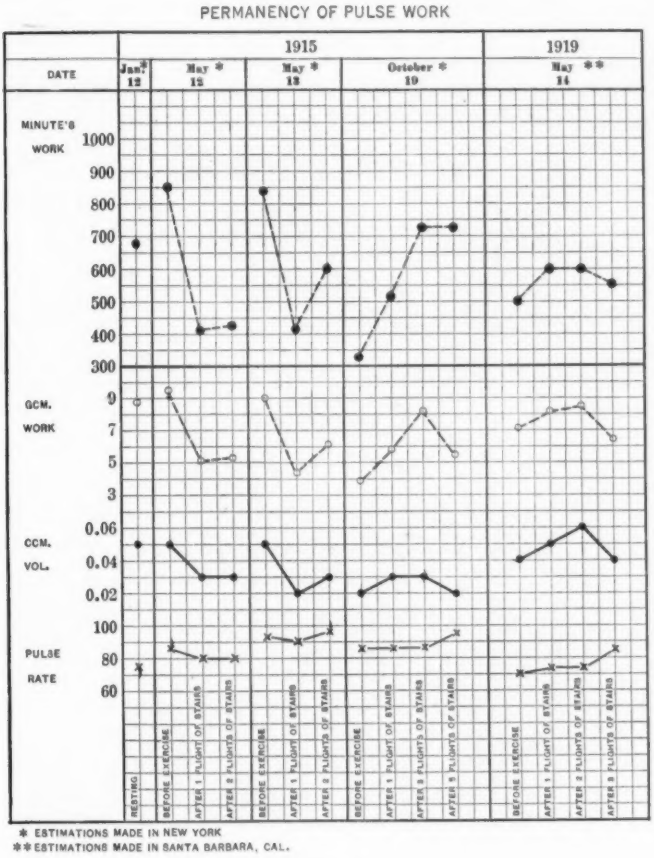
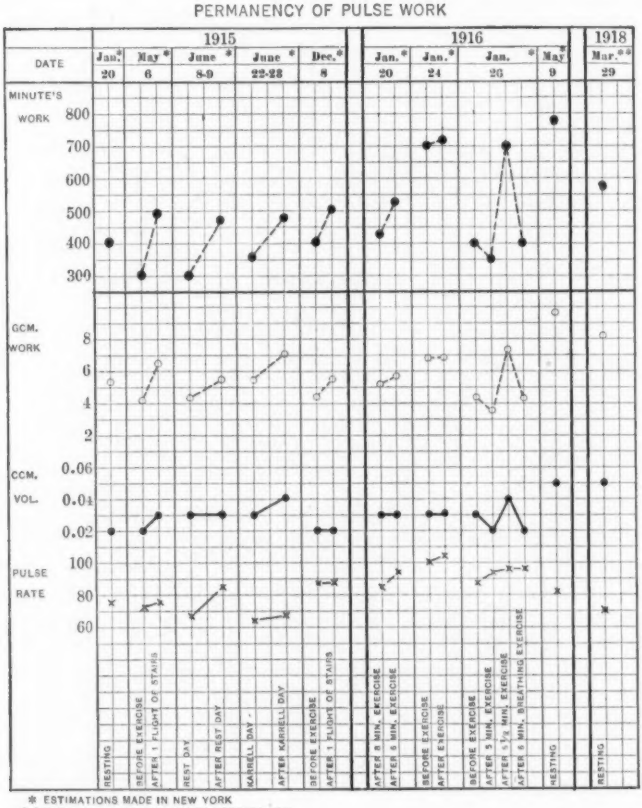


CHART 4

the difficulty is repeated at both the upper and the lower ends of the excursions, errors in reading of as much as 1 mm. may readily occur with rapid pulsation, and, *e. g.*, at an optimal pressure of 10 cause variations of about 2 g.cm. I attempted to facilitate the readings in very rapid oscillations by employing a diminishing loop

and so reducing the rapidity of the retinal impression, but the experiment had the drawback of diminishing at the same time the absolute measure. Errors may also arise if the system is not perfectly tight, and unnoticed the pressure gradually falls during the observations and the reflux index movement resulting from the falling of the pressure is then superimposed with consequent too



* ESTIMATIONS MADE IN NEW YORK
** ESTIMATIONS MADE IN SANTA BARBARA, CAL.

CHART 5

low values. In pressure bolometry this possibility of error is, on account of the smaller excursions, of greater significance than in volume bolometry. Besides, the optimal pressure frequently falls very rapidly without being noticed and too low values are thus read off.

"The most important cardinal points after all, are:

Insufficient tension of cuff;
Deficient rigidity of rubber tubing;
Loosening of the cuff;
Leaking in the system;
Reading errors on account of the rapidity of excursion and the obscurity of the index meniscus with the rapid movement.

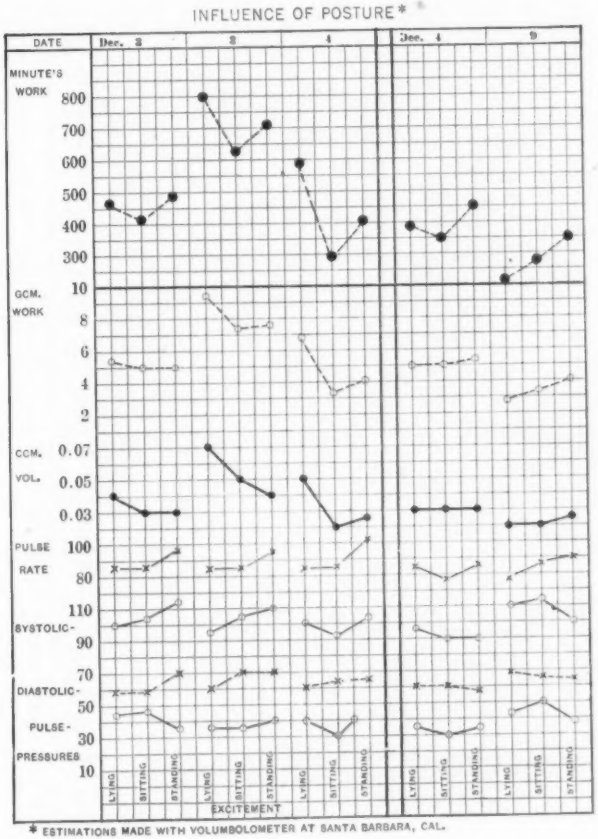


CHART 6

"In the final result of the estimated pulse work all these cause negative errors which are responsible for the unsatisfactory results that you describe. In general it is evident that with a strong pulse

and high values of pulse work the loss of energy is more difficult to prevent than with low values.

"It seems to me that you can very well utilize your own clinical observations in so far as they concern comparative observation on the same patient, but I should much regret your publishing incorrect

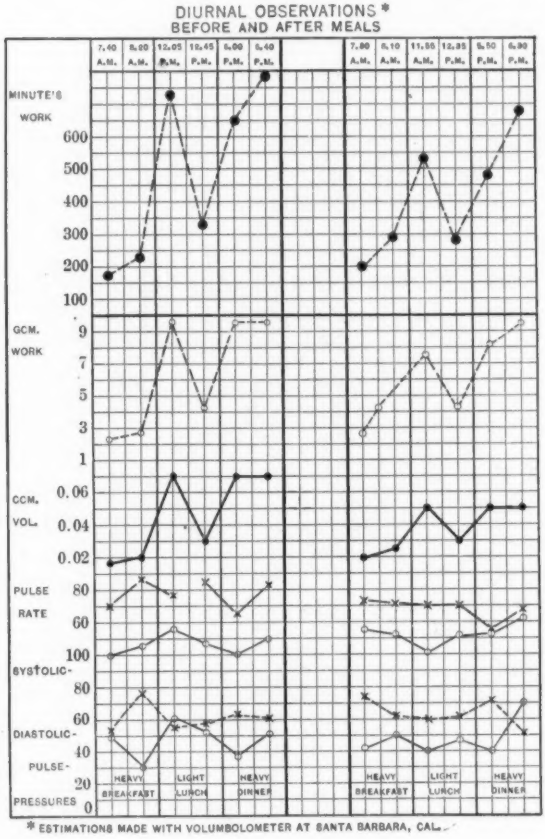


CHART 7

results, the cause of which errors I have just explained. Such results would better be withheld. Confusion would only result and not only pressure bolometry, but all sphygmobolometry be freshly discredited. The general medical public is neither discriminating nor sufficiently oriented to draw correct, even if not entirely erro-

neous, conclusions. Hence, I do not believe such an inclusion would accomplish the purpose mentioned in your letter, of furthering the method. Sphygmobolometry merits support, and although it has

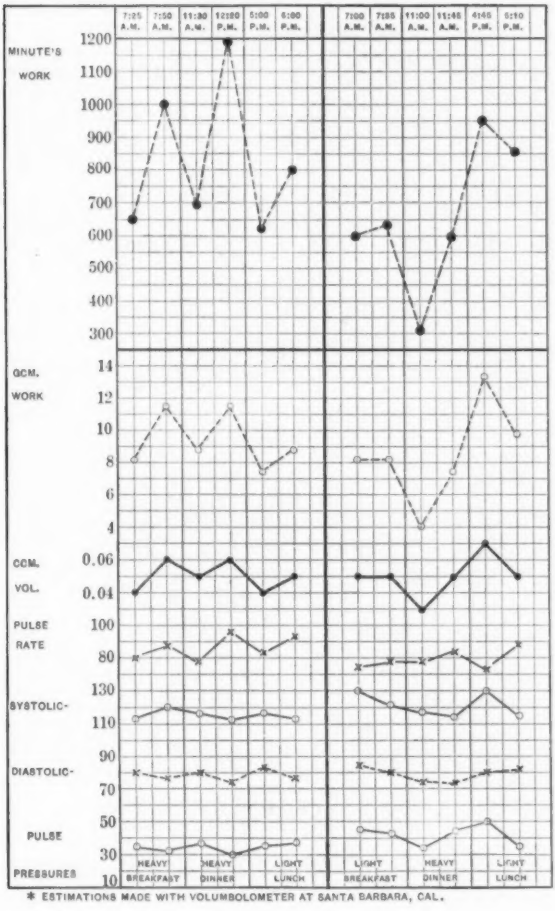


CHART 8

not yet attained an undisputed place in stricken Europe, it should acquire such recognition in unprejudiced America. For the moment most of the great medical public unintelligently regard the method

as entirely useless, but I am convinced that eventually sphygmobolometry will entirely reform clinical hydraulics, although by then I shall probably have passed away."

One final caution, from the patient's standpoint, is worth mentioning. I have repeatedly observed, especially in high strung, sensitive patients, with high blood-pressure and broad excursions

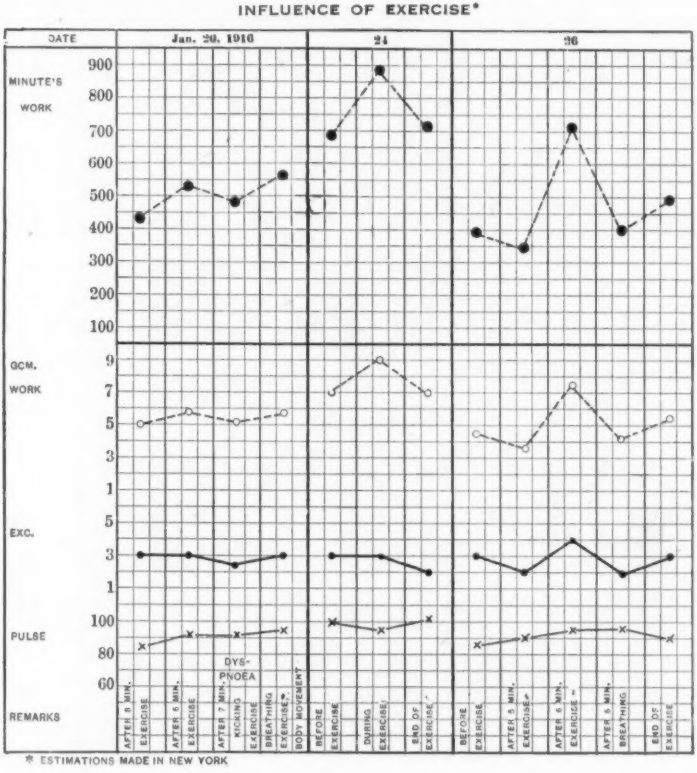


CHART 9

of the transmitted beat, so decided a trepidation, dread, or fear while watching this lively, extensive oscillation of their own pulses as to render any such series of determinations quite inadvisable from the point of view of their proper treatment. It seems to have quite the same effect as in the old days when similar patients builded their happiness or misery upon the presence or absence of albumin and casts in their urine.

PERMANENCY OF AN INDIVIDUAL'S PULSE WORK. Charts 4 and 5 tend to show that in the ordinary individual the figures for the Work or Volume do not vary to any striking degree, in the course of a brief number of years. Most of these observations were made

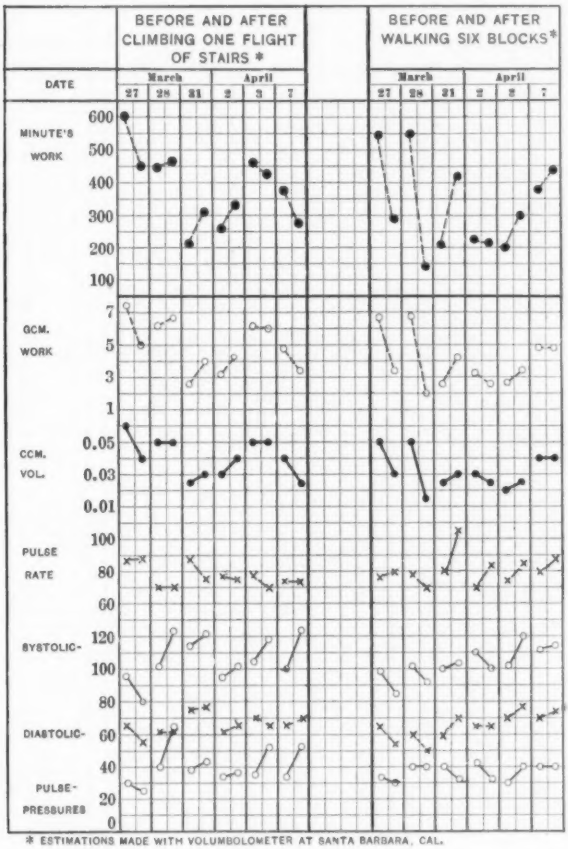


CHART 10

before and after various forms of exercise, and although the response to exercise may vary with variations in the patient's condition, the limits within which these variations occur remain fairly constant, in spite of the fact that observations were made both in New York

and in Santa Barbara, California, with entirely different instruments and several different observers.

VARIATIONS DEPENDENT UPON EXTRAMEDICINAL INFLUENCES. Pulse volume and heart work vary with the ordinary daily procedure and happenings of normal life, such as posture, activity, exercise,

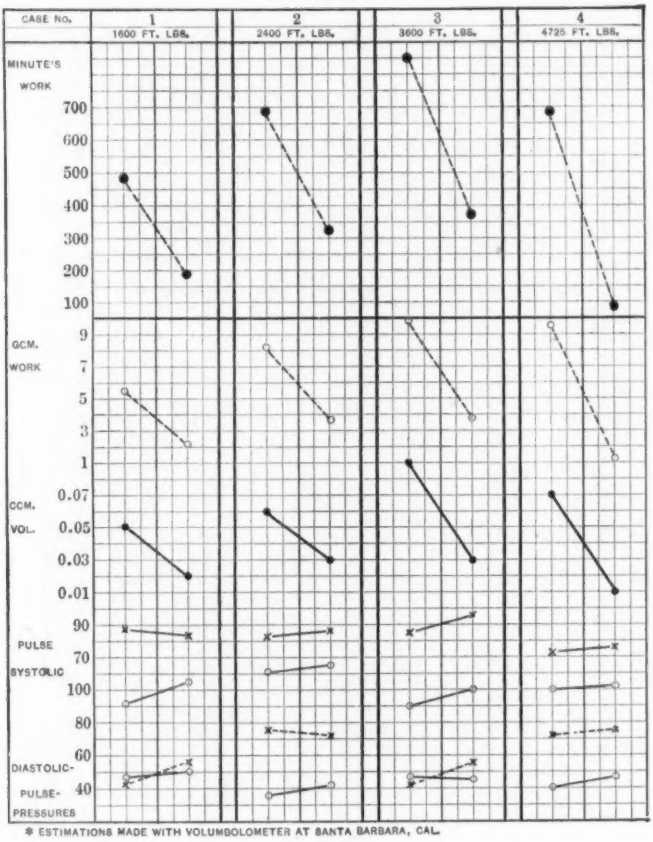


CHART 11

eating, drinking, bathing, nervous excitement, rest, fatigue, etc., so that to determine if one or both of these definitely measurable dynamic qualities of the pulse can be utilized in estimating circulatory efficiency, we have made a certain number of estimations upon

normal and diseased individuals before and after such influences. It ought to be helpful, for example, if a certain individual can run up so many stairs in a given time and show no effect of fatigue; and if an increase in the number of stairs, or the speed with which they are traversed results in a moderate increase in *minute work*, we would presumably consider the circulatory response as relatively efficient; but if, at the second flight of stairs, the *minute's work* which

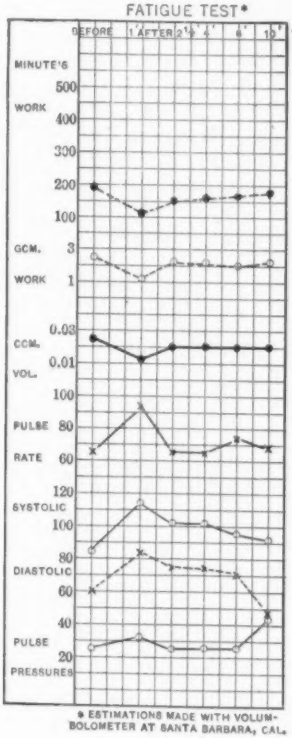


CHART 12

had been moderately increased after one flight, suddenly fell, and especially if at the same time the pulse-rate considerably increased, such a result would evidently mean fatigue, and point to a relatively inefficient circulation.

Chart 6 exhibits the difference in *minute's work*, in two normal individuals in the horizontal, sitting and vertical postures. In changing from a horizontal to a sitting posture there is typically a

considerable decrease in minute's work, which is usually brought about by a decrease in pulse volume. The minute's work increases again, however, when the subject assumes the vertical position.

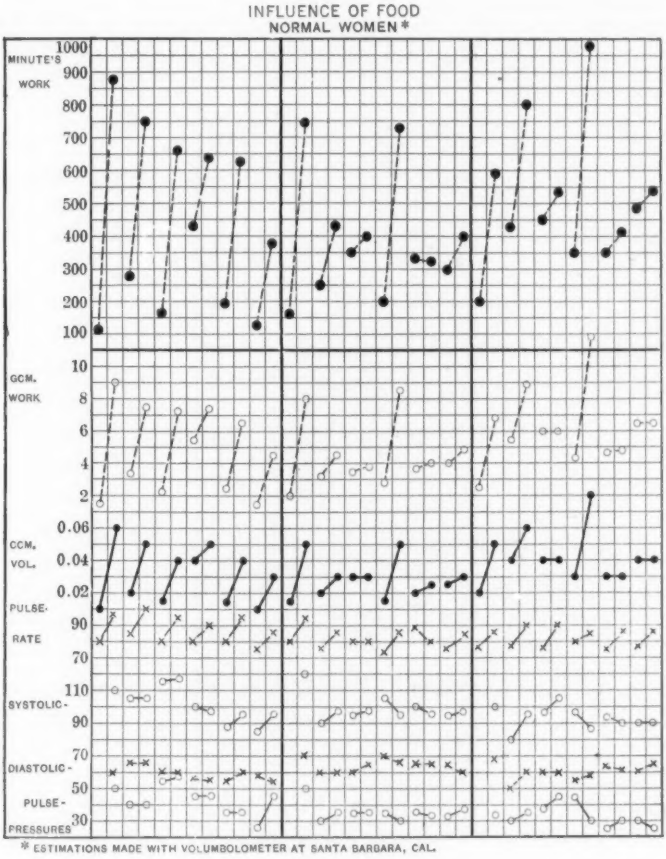


CHART 13

Charts 7 and 8 represent the difference in *minute's work* in four individuals in the early morning, before breakfast, after breakfast and before and after the midday and evening meals. The similarity of the curves in Chart 7 is quite striking. The lowest points of the curves of work, minute's work and volume are all at the early

morning reading. This is followed by a slight rise after the ingestion of food. The activities of the day and increase in temperature of a very relaxing summer day, result in markedly higher readings

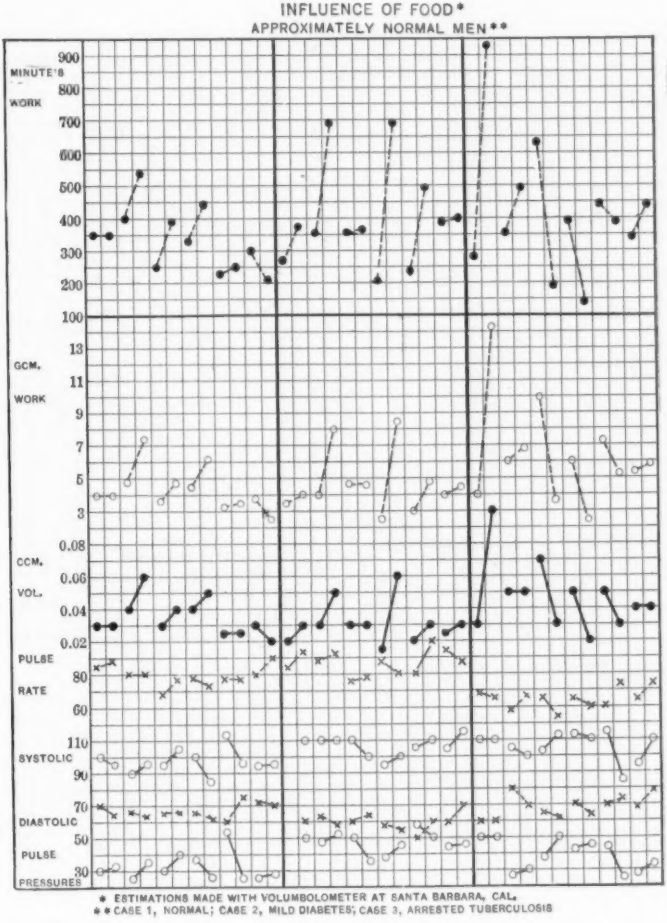


CHART 14

at noon, but these high readings are followed by a drop after the noon meal. In the evening again the readings are high, followed by a further increase in minute's work after the evening meal, this

increase being due to an increase in pulse-rate rather than to any change in volume. The observations illustrated by Chart 8 were made upon nurses, interrupted at their work, where influences other than food were probably present. There is, however, a general

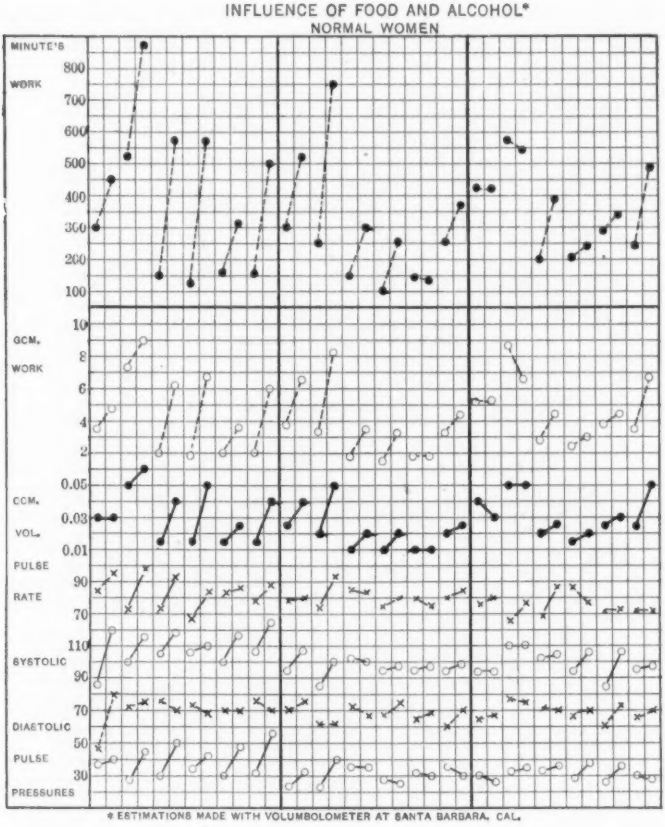


CHART 15

tendency for the minute's work to increase after meals. These observations were made on a cool, bracing day when there was little change in temperature during the day.

Charts 9 and 10 represent the effect of some different types of exercise in two normal individuals. Here the normal reaction to exercise is an increase in minute's work, generally accompanied by

a corresponding increase in gram centimeter's work and in volume. Where there is a decrease in minute's work it indicates fatigue.

Chart 11 shows the effect of fatigue on four normal subjects. The readings were taken before and as soon after exercise as it was

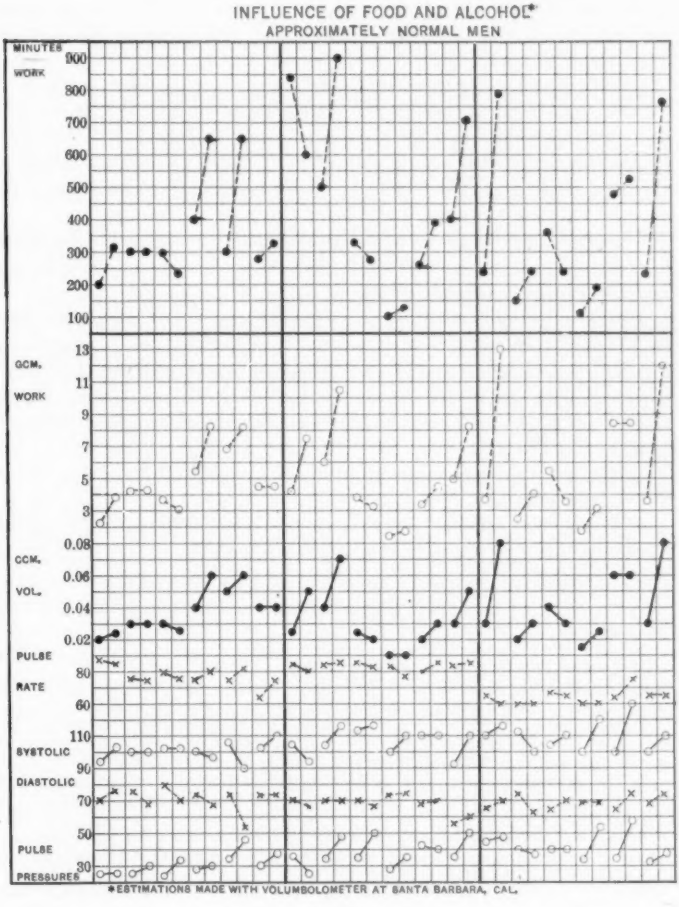


CHART 16

possible to adjust the cuff; thereby obtaining a marked decrease in work and minute's work.

Chart 12 shows the effect of fatigue and the gradual return to

normal after the initial decrease in work. Readings were taken at intervals of one minute, two and a half, four, six and ten minutes after exercise.

Charts 13 and 14 represent the effect of food in six individuals. There is generally a marked rise in minute's work, gram centimeter's work and volume after the ingestion of food; and this is especially well shown in Chart 13 where the subjects are more nearly normal than those of Chart 14.

Charts 15 and 16 represent the effect of food in these same individuals, under similar conditions, at the same time of day, when this food was supplemented by a certain amount of alcohol. There is less regularity in the results obtained in these two charts than in the two preceding, uncomplicated food charts, but the general or average tendency toward a rise after the meal is the same.

SUMMARY. 1. It is evident that the method of volume bolometry is relatively simple, easily applicable, not unduly time-consuming and of at least practical accuracy.

2. To determine whether the results obtained therefrom are sufficiently valuable either in estimating circulatory efficiency, *i. e.*, a functional circulatory test, or in following, or judging the effect of medicinal, or extra-medicinal methods of treatment, more clinical experience under a greater variety of conditions must necessarily be available.

3. It suggests a new conception of the circulation and certainly is worth further study.

4. It is better adapted to clinic or perhaps to office practice than to routine private practice at a patient's home.

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THE RAPIDITY AND PERSISTENCE OF THE ACTION OF DIGITALIS ON HEARTS SHOWING AURICULAR FIBRILLATION.[1]

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The fact that digitalis requires many hours or even days to affect the heart when given in the usual doses, has been perhaps the chief disadvantage in the use of the drug in cases of heart disease in which prompt action is urgently indicated. It is well known that repeated doses must be given before the action of the drug manifests itself, and it is often difficult to determine accurately when the action begins. There has also been considerable discussion as to how long the drug remains effective after its administration is stopped, a point of important bearing on the so-called cumulative action of the drug.

In order to gain further knowledge regarding these questions, the effect of large single doses of digitalis has been observed on a selected group of patients suffering from a form of cardiac disorder which is definitely influenced by the drug. All the cases studied were demonstrated by electrocardiograms to suffer from either auricular fibrillation or auricular flutter, and in all the ventricular rate was abnormally rapid. Care was taken in every case to make sure that the patient was not under the influence of digitalis when the large dose was administered, either by the history, or the statement of the physician sending the patient into the hospital, or by a period in the hospital of at least ten days without the administration of the drug.

Digitalis was given by mouth in the form of the tincture and the dose was regulated according to the method worked out by Eggleston.[2] The underlying principle of this method is to give in one or several frequent doses the entire amount of the drug which may be expected to produce the maximum therapeutic effect. The tincture of digitalis used was purchased from a reliable manufacturer and

[1] Read before the Association of American Physicians, Atlantic City, June 17, 1919.

[2] Digitalis Dosage, Arch. Int. Med., 1915, xvi, 1.

each lot of the drug was standardized by the "cat method," described by Hatcher and Brodie.[3]

It was found that 1 c.c. of the tincture injected intravenously was approximately the lethal dose for one kilo of body weight of the cats used, and following Eggleston's results, 0.15 c.c. was given for each pound of body weight of the patients. The dose, amounting to 15 c.c. per hundred pounds, was the maximum, and was usually given as a single dose, although in some of the earlier cases

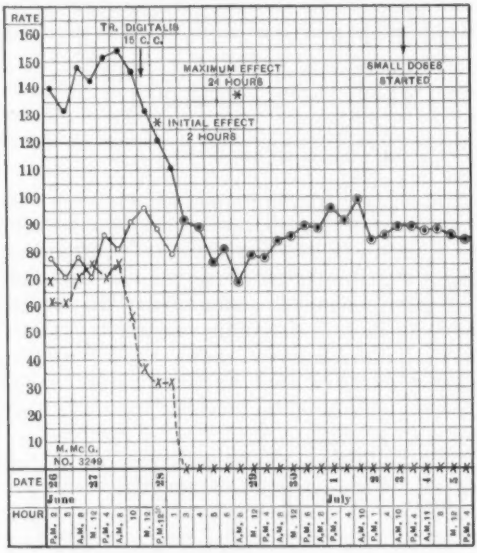

CHART I.—Case 9 of Table. Mitral stenosis and auricular fibrillation. The upper solid line indicates the heart-rate counted by means of the stethoscope placed over the apex-beat. The lower solid line indicates the radial pulse-rate. The broken line indicates the pulse deficit or the number of cardiac contractions that could be heard per minute, which produced no palpable pulsation in the radial artery. The time when the single dose of digitalis caused the initial and maximum effects are indicated. The increase in the rate of the radial pulse and the fall in the pulse deficit with the decrease in the heart-rate are well shown. Initial effect in two hours. Maximum effect in twenty-four hours. Duration of effect not determined.

the dose was divided into three or more parts and given four to six hours apart. The clinical results obtained in giving large single doses of the drug to about 100 patients have been convincing of the correctness of Eggleston's work. This will be demonstrated also by the cases tabulated in this paper. The doses usually ranged from 15 c.c. to 25 c.c. of the tincture.

The patients forming the basis of this paper were studied during continuous rest in bed. The heart rate was counted several times

[3] Biological Standardization of Drugs, Am. Jour. Pharm., 1910, lxxxii, 360.

a day by a member of the medical staff, using the stethoscope over the heart, for a number of days whenever the withholding of the drug seemed justified. The radial pulse was also counted, and these findings, together with the pulse deficit (the difference between the heart and radial rates), were charted. After the digitalis was given similar counts were frequently made, in some cases at fifteen-minute intervals, for several hours. The results of three observations are shown in the accompanying charts.

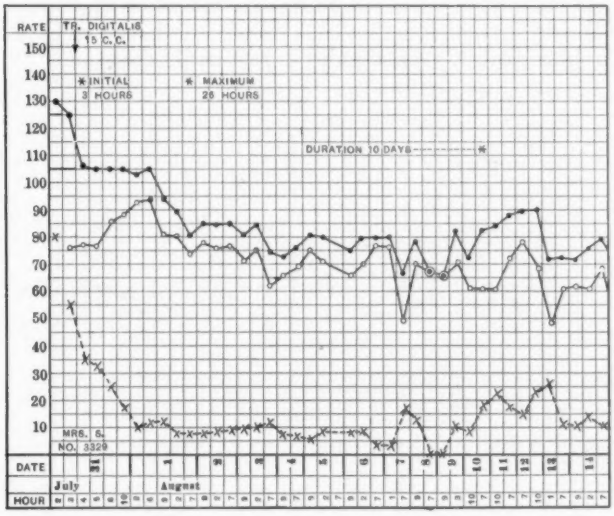

CHART II.—Case 11 of Table. Mitral stenosis and insufficiency, chronic myocarditis and auricular fibrillation. The three lines have the same significance as those in Chart I. The time when digitalis began to be ineffectual is indicated by the increase in the heart-rate which began ten days after the administration of digitalis. Initial effect in three hours. Maximum effect in twenty-six hours. Duration of effect ten days.

The well-known effect of digitalis in slowing the ventricular rate in cases of auricular fibrillation was used as indicating the action of the drug, and practically all of the cases included in this paper showed an abnormally high ventricular rate before digitalis was given. Two cases of auricular flutter are exceptions to the foregoing procedure, and here the disappearance of flutter, as demonstrated by electrocardiograms, was taken as evidence of digitalis action.

Twenty-six cases were studied and tabulated.

In 16 cases the observations were made at intervals sufficiently frequent after the single dose of the drug was given to determine accurately the time when the digitalis became effectual. The drug was considered to have affected the heart when the ventricular rate first became slower than it had been at any time previous to

the administration of digitalis and when the ventricular slowing continued, so that the rate of the ventricles assumed a definitely new level. In 2 cases the permanent disappearance of auricular flutter was taken as the indication that the drug had affected the heart. In all of the 16 cases so observed the heart was affected by digitalis in from two to five hours after the oral administration of a single large dose of the tincture.

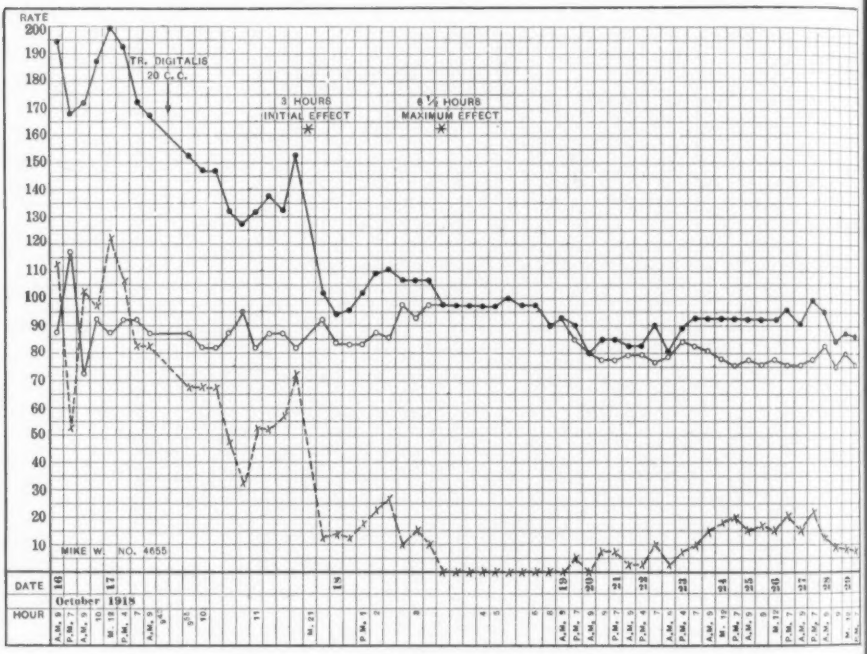

CHART III.—Case 25 of Table. Syphilis, chronic myocarditis and aortitis. The three lines have the same significance as in Chart I. Single dose of 20 c.c. of the tincture given. Initial effect in three hours. Maximum effect in six and a half hours. Heart-rate remained slow for twenty-two days.

The maximum effect of digitalis was considered to have occurred when the ventricles attained approximately their slowest rate and when the pulse deficit had disappeared or reached its lowest count. It was usually quite clear when the maximum effect occurred, but in some cases in which frequent heart-rate counts were not carried on long enough the maximum effect can only be approximated. The charts from the 26 cases studied indicate there is some difference in the length of time required for a single large dose of digitalis to produce the maximum effect on cases of auricular fibrillation, and the cases fall into two groups.

THE EFFECT OF A MASSIVE DOSE OF DIGITALIS ON CASES OF AURICULAR FIBRILLATION.

	No.	Sex.	Age.	Wt.	Diagnosis.	Dose.	Heart-rate.			Duration.
							Before.	Onset time.	Maximum effect.	
1	2608	M.	62	124	Arterial sclerosis; mitral insufficiency; chronic nephritis	17 c.c.	85	?	60, 24 hr.	7 days.
2	2178	F.	52	127	Arterial sclerosis; mitral insufficiency; chronic nephritis	18.5 c.c. in 4 doses	120	?	80, 20 hr.	8 days small doses started
3	2567	M.	48	172	Mitral stenosis and insufficiency	22 c.c. in 3 doses	160	106, 13 hrs.	80, 23 hr.	10 days.
4	2484	F.	49	151	Mitral stenosis and insufficiency; chronic nephritis	22 c.c. in 3 doses	142	105, 5 hrs.	92, 24 hrs.	6 days small doses started.
5	2589	M.	57	190	Mitral insufficiency; myocarditis; chronic nephritis	29 c.c. in 3 doses	135	?	76, 15 hrs.	3 days small doses started.
6	2819	M.	72	137	Arterial sclerosis; chronic nephritis	15 c.c. in 3 doses	130	?	90, 24 hrs.	8 days small doses started.
7	3115	F.	45	140	Myocarditis; chronic alternans; auricular flutter	20 c.c.	148	102, 3½ hrs.; flutter change d to fibrillation	90, 24 hrs.	13 days.
8	3132	M.	63	110	Arterial sclerosis; chronic nephritis	6 c.c.	132	80, 3 hrs.	80, 3 hrs.	5 days small doses started.
9	3249	F.	35	106	Mitral stenosis	15 c.c.	145	120, 2 hrs.	68, 24 hrs.	5 days small doses started.
10	3257	M.	57	138	Arterial sclerosis; myocarditis; chronic nephritis	9.5 c.c. 5 days after 19 c.c.	Flutter repl	aced by normal	rhythm in 3½ hr	s. after 9 days in hospital.
11	3329	F.	36	100	Mitral stenosis and insufficiency; myocarditis	15 c.c.	130–140	105, 3 hrs.	80, 26 hrs.	11 days.
12	3358	F.	47	110	Mitral stenosis and insufficiency; cystic goitre	15 c.c.	130–160	110, 3 hrs.	85, 22 hrs.	8 days.
13	3466	M.	54	156	Arterial sclerosis; myocarditis	10 c.c., 5 c.c., 3 days later	120	?	82, 18 hrs.	13 days after 2d dose.
14	3494	M.	37	135	Mitral stenosis and myocarditis	20 c.c.	120–150	?	84, 20 hrs.	5 days, 2d dose given.
15	3530	F.	49	130	Exophthalmic goitre; myocarditis	20 c.c.	110–125	?	95, 24 hrs.	6 days.
16	3741	F.	43	178	Mitral insufficiency	18 c.c.	112–160	90, 3 hrs.	80, 8 hrs.	2 days mechanism became normal.
17	3757	M.	49	139	Arterial sclerosis; myocarditis; mitral insufficiency	20 c.c.	120	108, 3 hrs.	87, 14½ hrs.	9 days, 2d dose given.
18	3937	F.	42	122	Mitral stenosis and insufficiency	15 c.c.	75–135	60, 3 hrs.	38, 2½ hrs.	15 days.
19	4018	F.	60	74	Mitral stenosis and insufficiency	6 c.c.	150–165	114, 2 hrs.	100, 21½ hrs.	4 days death.
20	4102	F.	23	132	Mitral stenosis and insufficiency; aortic stenosis	6 c.c.	95–115	80, 2 hrs.	55, 6 hrs.	10 days patient discharged
21	4190	M.	62	121	Myocarditis and chronic nephritis	15 c.c.	120–128	?	91, 8 hrs. 81, 26 hrs.	9 days patient discharged
22	4230	F.	54	198	Arterial sclerosis; myocarditis; chronic nephritis	10 c.c. 2d dose 10 c.c.	175–180	160, 4½ hrs.	120, 22½ hrs.	30 hrs., 28 hrs.
23	4261	M.	42	168	Myocarditis; syphilis	15 c.c.	150–175	105, 5 hrs.	90, 18 hrs.	
24	4449	M.	40	120	Mitral stenosis and insufficiency	20 c.c.	120–150	?	70, 24 hrs.	4 days.
25	4655	M.	48	165	Myocarditis; syphilis; aortitis	20 c.c.	135–160	118, 3 hrs.	112, 7 hrs.	6 days.
26	4977	F.	37	?	Mitral stenosis and insufficiency; myocarditis	15 c.c.	167–207	102, 3 hrs.	96, 6½ hrs.	22 days patient discharged
							130–140	110, 2¼ hrs.	70, 9 hrs.	4 days patient discharged.

In the first group of 19 cases the maximum effect of the drug occurred in from fifteen to twenty-six hours. In a second smaller group of 6 cases the maximum effect occurred in from six to nine hours. The cause of the difference between the two groups is not apparent. In a case of auricular flutter in which the normal cardiac rhythm supervened after digitalis was given no statement as to the maximum effect can be made.

In order to determine the length of time which the drug controlled the heart the patients were kept constantly in bed and the ventricular rates were counted by the stethoscope several times a day. When the ventricular rate began to accelerate and the pulse deficit to increase the drug was considered to have begun to be ineffectual. At this time another dose of digitalis, usually half the amount originally given, was followed by a prompt fall in the ventricular rate and in the pulse deficit. The rise in the ventricular rate was practically always accompanied by an increase in the symptoms of cardiac inefficiency.

In 12 cases in which the time when the drug began to be ineffectual was clearly indicated, digitalis affected the heart for from four to fifteen days, the effect lasting on an average of nine days and six hours. In 1 case the ventricular rate remained slowed for twenty-two days, when the patient was discharged from the hospital without receiving another dose of the drug, although the primary effect had been very striking. In another case the ventricular rate began to accelerate thirty and twenty-eight hours respectively after each dose of 10 c.c. of the tincture, given several days apart. In the remaining 12 cases no statement regarding the duration of the effect can be made, as subsequent doses of the drug were given before the effect of the initial dose had begin to diminish, or, as in 1 case in this series, the patient died four days after the initial dose.

From this series of cases it may be stated, however, that although the effect of a single large dose of the tincture of digitalis on the heart is not constant, it usually lasts from four to fifteen days, and averages nearly ten days.

The persistence of the action of digitalis is of considerable practical importance, and has been the subject of several investigations. Hatcher[4] has shown that various digitalins vary in their persistence in experimental animals and that the persistence also varies markedly in different animals. He showed that the effects of digitonin and digitalis persist longer than do those of the other digitalins in common use, especially in cats. He found that the effects of a single large dose of these drugs, administered intravenously, may persist for a full month. Cohn, Fraser and Jamison[5] investigated this subject, determining the persistence of the drug administered orally

[4] The Persistence of Action of the Digitalins, Arch. Int. Med., 1912, x, 268.

[5] The Influence of Digitalis on the T-wave of the Human Electrocardiogram, Jour. Exp. Med., 1915, xxi, 593.

to patients by the change in the T-wave of the electrocardiogram. They found that this change, which was brought about by digitalis, persisted for from five to twenty-two days after the administration of the drug was stopped. Although this method of determining the effect of digitalis was not consistently followed in our series of cases, the impression was gained from several cases so studied that the return of the T-wave of the electrocardiogram to the form present before digitalis was given occurred a day or two later than the acceleration of the ventricular rate.

Eggleston[6] has also been among those who have studied the duration of digitalis action in man. He determined the length of time that various cardiac disturbances produced by the drug persisted and found that coupled beats (regularly recurring premature ventricular contractions) persisted for from four to twelve days after digitalis was discontinued, while other disturbances of the cardiac mechanism caused by digitalis persisted for a shorter length of time.

A matter that has been frequently discussed regarding the effect of digitalis when administered by mouth has been the question of the rapidity of its absorption from the alimentary tract. The study of our series of cases seems to throw some light upon this subject. It has been customary to consider the absorption of digitalis from the alimentary canal as irregular, slow and uncertain and the factor of absorption has been called upon to explain differences in the amounts of the drug required to produce the same effects in different individuals. Recently, Wedd[7] found there was a wide difference in the amounts of digitalis necessary to produce certain toxic effects in different individuals, the individual variation being from 20 c.c. to 100 c.c. of the tincture given in large but not single doses. The variation, he believes, is due to variations in absorption. There is, no doubt, definite difference in the rapidity of absorption of different digitalis preparations, as Haskell, McCants and Gardner[8] have shown experimentally, and they find that the tincture is better absorbed from the gastro-intestinal tract than the infusion, and is equally as well absorbed as other preparations.

Eggleston concluded from his study of the effects of large doses of the drugs that digitonin was more completely absorbed than digitalis, but, nevertheless, he found that both of these preparations are probably rapidly and fairly uniformly absorbed from the alimentary canal of man.

The fact that a single large dose of the tincture of digitalis uniformly affected the heart of all of the cases in our series in which its

[6] Clinical Observations on the Duration of Digitalis Action, Jour. Am. Med. Assn., 1912, lix, 1352.

[7] Observations on the Clinical Pharmacology of Digitalis, Bull. Johns Hopkins Hosp., 1919, xxx, 131.

[8] The Rate of Absorption of Various Digitalis Preparations from the Gastro-intestinal Tract, Arch. Int. Med., 1916, xviii, 235.

initial effect could be determined in from two to five hours, offers a strong argument for the fairly rapid and uniform rate of absorption from the alimentary tract of patients with heart disease. It is true that the maximum effect did not show so uniform a relation to the time of administration, but it seems probable that factors other than absorption may have been responsible for the variations in the time required for the maximum effect to occur.

It is this rapid and uniform rate of action of the drug when administered in large single doses as herein described, which especially commends the use of digitalis in this manner therapeutically. It is felt that further studies are required before such large doses as were given should be recommended for general use, especially when patients are not under constant observation in hospitals. But the method has been sufficiently tried so that it seems entirely justified whenever rapid digitalis action is strongly indicated, and our experience leads us to believe that it is a much safer method of obtaining rapid digitalis action than the intravenous administration of digitalis bodies, especially strophanthin. Nearly all the cases reported in this series showed very striking clinical improvement within a few hours after the administration of the single large doses of the tincture of digitalis. It is particularly on this account that it is felt that Eggleston's conclusions as to the dosage of the drug are essentially correct.

SUMMARY. A series of 26 cases of auricular fibrillation or flutter are reported, to which large single doses of the tincture of digitalis were administered by mouth. The drug used was standardized and was usually given in doses ranging from 15 c.c. to 25 c.c.

The study of these cases demonstrates that such doses of digitalis affect the heart of cases of auricular fibrillation or flutter at a relatively constant time after administration, in from two to five hours, indicating that the drug is absorbed from the alimentary tract at a fairly rapid and uniform rate. The series of cases also demonstrates that the maximum effect on the heart is usually obtained in about twenty-four hours and generally continues to be effectual for from four to fifteen days, or on an average of nearly ten days.

REVIEWS.

EXPERIMENTAL PHARMACOLOGY. By HUGH MCGUIGAN, PH.D., M.D., Professor of Pharmacology in the University of Illinois, College of Medicine, Chicago. Pp. 250; 56 engravings; 7 colored plates. Philadelphia: Lea & Febiger, 1919.

THIS is, to quote the author, "an attempt to present experimental pharmacology in a brief, concise form, yet give the student an adequate view of the field." The book contains a summary of the main facts of pharmacology, in outline form, with directions for illustrative experiments, arranged with regard to the action of drugs on the various physiological systems. The introductory chapters contain general information to be found in standard text-books, and will be valuable to supplement a course of didactic instruction. The outlines of major facts of pharmacology suggest the "quiz compend" method and are not conspicuously good. Accompanying these outlines are directions for some 320 illustrative experiments, the performance of all of which, while of undoubtedly great value, would be quite beyond the time available in the usual course of instruction. The author, however, suggests elimination or division, but does not indicate clearly just how this can be accomplished so as to return the greatest possible benefit to the student. The arrangement is at times unusual: the anesthetic action of ether and chloroform and the action of the alcohol-chloral group on reflexes are discussed with digitalis and the nitrites under Pharmacology of the Heart and Blood-pressure; experiments with bromides and cannabis are given in the chapter on the closed method of anesthesia; epinephrin is listed in the chapter entitled antagonism. Few experiments of an analytical character are included, most of them being aimed rather at an exposition of the action of the drug than an analysis of the precise method in which these effects are produced. The chief fascination of pharmacology, as a field of investigation, lies in experiments of the latter type, and it is unfortunate that the student entering this field for the first time should be left unaware of its legitimate pleasures. Nevertheless, these criticisms aside, the book is decidedly a departure in the right direction. It emphasizes to the student the value of experimental pharmacology and furnishes a much needed scientific background for the study of applied therapeutics.

C. F. S.

PHYSICAL DIAGNOSIS. By RICHARD C. CABOT, Professor of Medicine, Harvard University. Seventh edition. Pp. 527; 263 figures and 6 plates. New York: William Wood & Co., 1919.

THIS book does not need an introduction, as it has long been recognized as one of the foremost books upon physical diagnosis. It is founded upon good, sane clinical judgment with two underlying basic principles, thoroughness and common-sense. Dr. Cabot puts forth the basic principles of physical diagnosis, and in no case does he claim overexaggerated evidences from any one physical finding.

In this volume much new material has been added. Cardiac signs of nervousness as examplified by the D. A. H. cases are given the proper interpretations. It is pointed out that the simple goitre will sooner or later cause cardiovascular changes similar to those due to syphilis or other causes. This is always associated with an elevation of the systolic pressure with myocardial changes and of very slow development (average fourteen years). The diastolic pressure in these cases remains little if at all elevated. In the toxic goitre these changes are more rapid and usually come on within a year. Dr. Cabot again puts forth the growing idea that in the rheumatic endocarditis cases there is always an association or combination of stenosis and regurgitation. He also goes further and believes that practically all these cases are due to some variety of the streptococcus. Hilus tuberculosis is brought into a place of importance but again the word of caution is given that unless there is an association of symptoms the diagnosis should not be made as to its being active. It is pointed out that these are childhood infections, starting in the deep tissues around the hilus and there remaining dormant until adult life is reached. This is undoubtedly one of the most important factors set forth in the book, as these comprise a large number of the so-called "closed cases of tuberculosis" discovered in the course of a roentgen-ray examination.

It is to be regretted there are so many typographical errors in this most important book, but, nevertheless, this does not detract from the vast amount of most important knowledge contained therein.

T. K.

THE FUTURE OF MEDICINE. By SIR JAMES MACKENZIE, Consulting Physician to the London Hospital. Pp. 238. London: Oxford University Press, Henry Frowde and Hodder & Stoughton, 1919.

THIS little volume comes at the close of the active career of one of the foremost clinicians and investigators in clinical medicine now living. He has detailed the circumstances that led him to undertake his researches and the methods employed in carrying them out.

He has found much to criticise in medical education, research and clinical medicine as conducted at present.

The principal point of attack has been on the so-called ideal of medicine, dominant today, which is alleged to depend upon the revelation of the signs of disease by some mechanical contrivance devised in the laboratory. This trend in modern medicine has been vigorously protested against on the ground that not only is the knowledge to be gained by laboratory methods liable to be misleading if not carried on in conjunction with careful clinical observation, but that what value it has is limited to the late stages of disease after structural signs have developed. Real progress depends upon the detection and study of disease in earlier stages. Our medical education and research should therefore be adjusted to this viewpoint, and the study of symptoms, which are at present little understood, should assume the position of great importance it deserves. The general practitioner is said to have the best opportunity for research, and he should be educated to take advantage of his opportunity. In the hospital the out-patient department should receive the attention of the trained physician, for here he can study the beginnings of disease; in the ward he finds the end-results.

No one interested in medicine will fail to find much of value in this book. Many statements will encounter more or less general dissent, such as the claim that laboratory training unfits men for work as physicians. Nevertheless, the position and attainments of the author have enabled him to point out, as perhaps no other could have done, the dangers of subservience to laboratory methods; the fallacy of attempting to draw deductions of clinical application from data obtained solely by mechanical contrivances; the importance of directing our energy to studying the beginnings of disease and the value of methods, which in his hands, have led to such important contributions to medical knowledge. C. C. W.

THE WHOLE TRUTH ABOUT ALCOHOL. By GEORGE ELLIOT FLINT. Pp. 294. New York: Macmillan Company, 1919.

HERE are set forth the views and experiences of one who is greatly impressed with the virtues of alcohol. To quote his own words: "Alcohol does not ruin men, men disgrace alcohol. Alcohol does not produce deficiency; but original deficiency seizes upon alcohol and abuses instead of uses it, thereby perhaps increasing the original deficiency." Throughout the book, as the author discusses the various phases of the subject, he repeatedly returns to this idea, and for him this constitutes the whole truth.

W. H. F. A.

HINDU ACHIEVEMENTS IN EXACT SCIENCE. By BENOY K. SARKAR, Professor, National Council of Education, Bengal. Pp. 82. New York and London: Longmans, Green & Co.

THE great debt which the medicine of Western Europe owes to Arabian culture is generally acknowledged. Not so well appreciated is the fact that in many scientific matters the Hindus anticipated the Saracens, and in fact taught them. By the aid of human dissection, acquaintance with many drugs and a definite system of medical instruction the Hindus had made considerable advance in the natural history and treatment of disease while Europe was still sunk in superstition and barbarism. This book is a brief account of the scientific achievements of this old civilization and is of historical interest. W. H. F. A.

PSYCHOSES OF THE WAR. By H. C. MARR, M.D., Lieut.-Col., R.A.M.C.; Fellow of the Royal Faculty of Physicians and Surgeons, Glasgow. Pp. 272; 60 illustrations. London, England: Oxford University Press, 1919.

THE author emphasizes the fact that no new types of mental disorders were brought to light in the recent war and no new technic of treatment evolved. However, in his study of over 18,000 cases of mental affections divided among officers and enlisted men of the British Army observed during the entire period of the war, he obtained much information upon mental conditions which, although recognized prior to the conflict, had been insufficiently investigated because of scarcity of cases. As a consequence the author has evolved a classification of mental affections which differs somewhat from those of our present accepted authorities.

Colonel Marr has apparently given great care to the construction of the book, which shows evidence of not having been very hastily written, as so many of the recent war books do. He cites many typical case histories as illustrative of the various types of mental and nervous disorders discussed. These add greatly to the clinical interest and aid in making the author's rather unique classification of mental affections more acceptable to the reader.

The book is in seven chapters, the first being an introduction dealing with the subject as a whole, the article on malingering and its detection being of particular interest. The second deals with the psychopathies, or the hereditary and constitutional psychoses. The third is devoted to a study of psychasthenia. The fourth and fifth, respectively, to mental deficiency (infantile) and mental enfeeblement (adolescent). The toxic psychoses (the confusional insanities) are discussed in the sixth and the organic psychoses ("the cerebropathies") in the seventh. A short appendix, dealing

with the nature and method of examination of the cerebrospinal fluid, is of interest to the student, as is also a very complete and ingenious diagram for mental case taking, which is appended after the index.

As a whole, the book will be of value to those who will have the opportunity of observing the many recurrent cases that will appear in civil practice following the closing of the army mental hospitals. It is also of value as a history of the types of mental affections which were dealt with in the great war. F. H. L.

THE ANATOMY OF THE PERIPHERAL NERVES. By A. MELVILLE PATERSON, M.D., F.R.C.S., Professor of Anatomy in the University of Liverpool. Pp. 165; 64 illustrations. London: Oxford Press, 1919.

THIS presentation of the subject of peripheral nerves was conceived by the late Professor Paterson while occupying the position of Assistant Inspector of Special Military Surgical Hospitals during the war. The object was to provide a brief account of the peripheral nerves, especially for those engaged in military orthopedic work. To this end are introduced schemata giving the position of origin of the branches of the nerves to the limb muscles. These are in the form of full-page line illustrations and achieve their purpose very well, although, as the author points out, they must be used with due caution. Useful diagrams are shown of the innervation of the skin and of the muscles of the limbs. In each of these, alongside the illustrations is given the name of the nerve and also the spinal segments from which its fibers are derived. This linking up the name of the nerve with its spinal origin is carried out consistently through the book. In addition to the subject of spinal nerves, which takes up the major part of the book (87 pages), a short consideration is given of the sympathetic system (20 pages) and of the cranial nerves (50 pages). W. H. F. A.

A LABORATORY MANUAL FOR ELEMENTARY ZOÖLOGY. By L. H. HYMAN, Department of Zoölogy, University of Chicago. Pp. 140. University of Chicago Press, Chicago, 1919.

AN important feature of the premedical education in college is the study of zoölogy with laboratory exercises. The course with which premedical students usually begin is that of so-called elementary zoölogy. This introduces them to the actual seeing and manipulation of various forms of animals, and usually requires also the use

of the microscope. To guide and direct the hands and eyes of these beginners and to forestall some of the oft-repeated questions is the purpose of the present manual. That it will achieve its purpose seems without doubt, for there is a terseness and directness of expression that is unequivocal, and each direction is given in logical sequence. While primarily for the use of students at the University of Chicago, it could be utilized readily elsewhere. W. H. F. A.

THE MEDICAL AND SURGICAL ASPECTS OF AVIATION. By H. GRAEME ANDERSON, M.B., C.H.B., F.R.C.S., Surgeon, Royal Air Force, Central Hospital; Senior Assistant Surgeon, St. Mark's Hospital; Senior Assistant Surgeon, Belgrave Hospital. Pp. 255; 47 illustrations. London: Oxford Medical Publications, 1919.

THE first book to make its appearance after the World War is on a subject which received the most intense study during hostilities by groups of experts in all countries. Surgeon Anderson was what we called in our service a "Flight Surgeon," and in his book he has given us the results of his work with the flyers, the actual application of the various tests which were devised to prevent, as far as possible, airplane accidents and the onset of aëroneurosis. His observations throughout the book are very practical and his recommendations for prevention and treatment of each type of case arising in the flying service are well considered.

He deals with the selection of the flyer *per se* and with the management of the pilot after entering the service, from his training days to actual war-flying and his care and management after he has become "stale" or injured.

Collaborating with him, with chapters on applied physiology of aviation and the aëroneuroses, are Martin Flack, M.A., M.B., and Oliver H. Gotch, M.B., Ch.B., M.R.C.P., physician, Royal Air Force, respectively. Martin Flack (Physiology, Cambridge) was the foremost investigator in the new field of aviation medicine in England. His tests were adopted as standards and his tireless energy and enthusiasm had much to do with the success in selecting the wonderful personnel of the Royal Air Force.

In the future development of commercial aviation the problems of the flyer will more and more become of interest to the medical profession, and in this book the future "flight surgeons" will find a great many helpful suggestions. Starting with a historical review of medical interest in aviation, and giving the English standards for selection of candidates for the air service, together with the special chapters on applied physiology by Flack and the aëroneurosis by Gotch, Anderson then gives his experiences in aëroplane accidents,

beautifully illustrated by actual plates, including a photograph of the most remarkable accident which has occurred in which a sea-plane collided with and stuck in the mast of a large wireless station. A chapter on the surgery of aviation, in which he fully reports, with roentgen-ray plates, thirteen cases of "aviator's astragalus," is important.

Chapters on injuries and destructive effects of aeroplane bombs, on aëroplane dope-poisoning (tetrachlorethane poisoning, which is used in waterproofing the wings, etc.), together with a glossary of aviation terms and a complete bibliography of aviation medicine to date, complete this valuable book. R. S. McC.

THE OPERATIVE STUDY OF GOITRE. THE AUTHOR'S OPERATION. By WM. F. HALSTEAD. Johns Hopkins Hospital Reports., Vol. XIX, Fasciculus 2. Pp. 257; 11 plates. Baltimore: Johns Hopkins Press, 1919.

HERE is told the tale of the surgeon's struggle, through many decades, to deal successfully with goitre, his failures, his partial successes and his ultimate achievement, a tale culled from wide reading in many languages and a long, broad personal experience. While the book undoubtedly will remain the authentic reference work on the subject, we believe it will not attract the many readers who expect in a book of this sort an entertaining story easily read; the "story" is too disjointed, too much a patchwork for enjoyment as a story.

The author has carefully set down synopses of all known operated cases until 1883 except for the German-speaking countries whose cases are too numerous for tabulation. Probably the earliest operation was in 1596. Although Hedenus did six excisions in the early 19th century and spilled very little blood, lay and professional opinion was strongly against surgical interference except in most urgent cases of dyspnea, until as late as 1870. It was massive hemorrhage that first checked all surgical efforts. In 1845 the Italian Porta ligated both superior and inferior arteries to cause atrophy of the gland and in 1862 the American Cooper used mass ligatures to cause reduction by sloughing. In 1866 his fellow countryman, Warren Greene, did perhaps the most important work in hemostasis. With the control of hemorrhage, the discovery of anesthesia and the acceptance of Listerism, the three greatest problems of surgery were solved and it remained to learn that in operation was a cure for hyperthyroidism, that total extirpation of the gland was followed by hypothyroidism and often by tetany and vocal cord paralysis, and finally there were developed refinements in technique, in instruments, incisions, approach to the gland and in the surgery of the

gland that placed thyroid surgery on sure ground. The greatest strides in these matters were made between 1878 and 1883 by Billroth, von Bruns, Reverdin, Mikulicz and preëminently by Kocher. The book closes with a brief statement of the author's original and important contributions to the technic of thyroid surgery. J. A.

War Neuroses and Shell-shock. By Frederick W. Mott, M.D., LL.D., F.R.S., F.R.C.P., Brevet Lieut.-Col., R.A.M.C.; Senior Neurologist to the Maudsley Neurological Clearing Hospital, London, England. Pp. 328; 3 original colored plates and 93 illustrations. London: Henry Frowde, Oxford University Press, 1919.

Colonel Mott has written many articles during the war dealing with nervous and mental disorders which he came in contact with in his army hospital services. In this volume he treats on the types, causation and treatment of the various forms of "war neuroses." His studies of actual shell-shock, resulting in death without external evidence of injury, are very well presented and illustrated. He differentiates "commotional" and "emotional" shock, and quotes several of the continental authors in support of his view. In the group of the psychoneuroses he found an acquired or inborn predisposition of emotivity in a high percentage of the cases. He believes that these men did not make good front-line material and that much expense and loss of man power could have been saved to the army had they been weeded out by a more thorough medical examination by the recruiting boards. He considers a neurosis as a subconscious defence reaction to an intolerable situation, and in support of his view states that most cases of war neuroses were not associated with external wounds, and, *vice versa*, that men with somatic wounds rarely developed neuroses.

As to the true psychoses of war the author states there are none and gives many excellent arguments and facts in support of this view. The types and frequency of psychoses correspond approximately to those of peace times.

The treatment as outlined is brief and exact, but leaves much to the imagination of the reader.

The one criticism of the book is the confusing way in which the author has assembled the whole. Had the presentation been systematic the book would be much easier to read and to understand.

As a whole the volume is one of the best that has been written dealing with the neurological problems arising in the recent war.

F. H. L.

PROGRESS
OF
MEDICAL SCIENCE

SURGERY

UNDER THE CHARGE OF

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War Wounds of the Joints.—DELREZ (*Arch. Méd. Belges*, May, 1919, p. 513) says that of 190 joint wounds treated within one year, 21 were infected and of these 16 involved the knee-joint. Under treatment he discusses only these 16. Five cases of purulent arthritis were treated without mobilization, the results being as follows: One was amputated with cure, 4 being resected. Two of the resected cases died and 2 were cured, with ankylosis. One of the 2 cured cases had a streptococcic septicemia after the resection. Of the cases treated by arthrotomy and mobilization there were 3 with staphylococcic serous arthritis in which there was complete cure, with total preservation of motion. In 4 cases of purulent streptococcic arthritis normal or very extensive motion was obtained. In an eighth case (streptococcic infection) death occurred on the tenth day from cardiopulmonary complications. In a ninth case with osteo-articular wound of the knee (streptococcic infection), osteo-articular wound of the elbow and multiple wounds of the soft parts the condition of the patient was so feeble as to call for amputation on the twenty-second day. In the tenth case (streptococcic) extensive destruction of muscles by gas gangrene rendered active mortification impossible. Prolonged efforts were followed by cure with partial mobility. In the eleventh case active mobilization was equally impossible, and, as in the previous case, passive mobilization was practised, so that after prolonged treatment and the help of an apparatus fair function was obtained. This (the Willems) method of treating joint infected wounds by active mobilization has furnished very satisfactory results.

Blood Transfusion as a Therapeutic Aid in Subacute Sepsis Associated with War Injuries.—ZINGHER (*The Military Surgeon*, 1919, xlv, 75) says that blood transfusions should be used more extensively on the wounded soldiers in the base hospitals. Officers should be especially

assigned to this work in the different base hospitals and base hospital centers, whose duties would be in connection with the performing of transfusions, consultations on medical and surgical cases and the keeping track of suitable donors. The special indications considered here are subacute sepsis, associated with extensive suppurations or with infected compound fractures, with anemia and emaciation of varying grades; also as a prophylactic measure in enfeebled individuals before severe operations and in cases of postoperative surgical shock resulting from extensive loss of blood during operation. Large pockets of pus, suppurating joints or extensive empyemas must, of course, be incised and drained. No blood transfusion will help in the elimination of these sources of continuous reinfection unless they are carefully watched for and taken care of as they arise. Autopsies often bring to light such complications, which should have been taken care of while the individual was still alive. The transfusions should be of moderate amounts of blood, from 250 to 300 c.c., and repeated, if necessary, every seven to fourteen days. Systematic efforts should be made to find these patients in the base hospitals. Special studies should be made and records kept after the transfusions, so as to obtain, as soon as possible, tabulated data that will help in more definitely indicating the value of blood transfusion in cases of subacute sepsis associated with extensive wounds and fractures.

Knee-joint War Injuries, with Report of 82 Cases Treated by Willems' Method.—McWilliams and Hetzel (*Annals of Surgery*, 1919, lxx, 257) says that in the management of septic cases as soon as frank pus is evident, either by signs of inflammation or bacteriological examination, thorough drainage must at once be established by vertical external and internal incisions. The joint is washed out thoroughly with Dakin's solution at the time of operation. Tubes had preferably not be used at first but may be later, if drainage is found to be insufficient. When they are used, the internal ends should project just inside the synovial membrane and no further. The after-treatment is conducted exactly as in the case of non-infected joints by active (not passive) motions carried out to the point of pain. These are begun immediately after the anesthetic has worn off and are repeated every two hours thereafter day and night. Even a day's delay will prejudice the final functional result. Walking is important because the muscular contractions compress the joint and cause a marked increase in the expulsion of the pus. The patient is made to walk the next day after the operation without crutches. It is surprising how much pus will exude from the incisions after each walk. It is very important that sufficient drainage openings be made to allow for an adequate escape of pus. These openings should be sutured just as soon as the discharge becomes serous. If the active motions are performed often enough and vigorously enough, these secretions are expelled through the drainage openings as they are formed. Drainage seems to be more thoroughly accomplished by this method than by any other, thus limiting the infection to the synovial membrane and tending to prevent its spread to the cartilage and bones. In civil injuries the results of operations with débridement, joint closure and immediate subsequent mobilization should be much better than in war injuries, because the patient is operated on more quickly, the infection

is not so virulent, there is no transfer to another hospital, and, finally, the after-nursing should be more effectively done. He concludes that no joint injury should be evacuated within ten days after the operation. The joint should be completely closed at the operation. No splint should be used except in those cases where fragments will be displaced. The Willems after-treatment of immediate, continuous, active movements should be unceasingly kept up day and night both in the aseptic and septic cases. In each hospital there should be a day and a night nurse who should be conversant with the method and whose only function it should be to carry out the active motions.

Fracture of the Acetabulum with Intrapelvic Displacement of the Femoral Head.—PEET (*Annals of Surgery*, 1919, lxx, 296) says that this fracture with central dislocation of the femoral head has a high mortality and is fortunately rare. Depression of the trochanter and rectal palpation of the femoral head are important diagnostic signs, but every case should be roentgen-rayed. Complications are frequent, severe in nature and demand immediate recognition and treatment. The successful repair of the fracture dislocation depends much on its early diagnosis. Reduction by manipulation is recommended. Open operation is necessary only in the exceptional case or for the treatment of complications. Resection of the femoral head is unnecessary. Manipulation under general narcosis, when the dislocation is unreducible, has yielded excellent results in freedom of motion and capacity to use the leg.

THERAPEUTICS

UNDER THE CHARGE OF

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The Treatment of Serofibrinous Pleurisy by Artificial Pneumothorax. WEIL (*Traitement des pleurésies sérofibrineuses par la pneumoséreuse thérapeutique* (*Bull. de l'acad. de Méd.*, 1919, lxxxi, 846) recommends injection of air into the pleural cavity after every puncture for serofibrinous pleurisy. The main benefit is that of preventing subsequent adhesions and the secondary difficulties that may develop. Of 86 cases of serofibrinous pleurisy subjected to puncture alone, 72, or 84 per cent., showed marked secondary trouble a few months or weeks later. Of 50 cases, on the other hand, in which puncture was followed by air injection 41, or 82 per cent., recovered without adhesions. In the 9 cases that did show pleural adhesions, the affection was of long standing before treatment was instituted. Seventeen cases out of the 50 treated with

injection of air recovered completely in from two to three months after a single injection. Fever and the other signs of infection rapidly disappeared, and most of the patients gained from 10 to 15 pounds in weight. A few recovered in less than a month. Thirty-three cases required more than one injection, but recovery, though more delayed, was as complete as in the cases requiring but a single injection. In cases where there is a rapidly recurring effusion, recovery is much delayed but this is possible after prolonged treatment. One such patient recovered in a year, having received in that time ten injections. One great advantage of the injection of air is that when pulmonary tuberculosis is the underlying cause of the pleural effusion, the effect of the induced pneumothorax is an arrest of the tuberculous process. It is most important to control such treatment by the roentgen ray and Weil's work was carefully controlled by radioscopy.

The Use of Benzyl Benzoate in Dysmenorrhea.—LITZENBERG (*Jour. Am. Med. Assn.*, 1919, lxxiii, 601) writes concerning the effect of benzyl benzoate in dysmenorrhea and reports inconclusive results regarding its value. He tried it in a series of 43 cases, in which 81.3 per cent. were relieved. Pain was absolutely eliminated in 62.7 per cent.; greatly relieved in 18.5 per cent.; slightly benefited in 4.6 per cent. These results, while not conclusive, warrant a more thorough test of the value of benzyl benzoate in dysmenorrhea. Benzyl benzoate is irritant when administered by mouth and should be given in capsules, well diluted with water, or as a 20 per cent. emulsion with acacia (this last preparation was found to be the most satisfactory). The dosage recommended by Macht proved insufficient, so Litzenberg finally increased the dose to 2 drams every two hours. No bad effects were observed, unless an occasional case of vomiting and rarely a feeling of weakness might be attributed to the drug.

A Therapeutic Study, Pharmacologic and Clinical, of Benzyl Benzoate.—MACHT (*Jour. Am. Med. Assn.*, 1919, lxxiii, 599) describes a number of clinical conditions that have been treated with benefit by benzyl benzoate. They may be summarized as follows: (1) Excessive peristalsis of the intestine, such as diarrhea and dysentery. Here, truly remarkable results were obtained; diarrheas of long standing were quickly checked and even dysentery was benefited by it. (2) Intestinal colic and enterospasm. (3) Pylorospasm, whether functional or reflexly produced by ulcers, etc. (4) Spastic constipation, in which there was a tonic spastic condition of the intestine. (5) Biliary colic. (6) Ureteral or renal colic. (7) Vesical spasm of the urinary bladder. (8) Spasmodic pains originating from the contractions of the seminal vesicles. (9) Uterine colic. (10) Arterial spasm, including a large number of cases of hypertension. The lowering of blood-pressure produced by benzyl benzoate was more lasting than that produced by administration of the nitrites. (11) Bronchial spasm. Wherever there were signs of bronchial constriction or spasm, benzyl therapy produced relief in almost every case. The theory of the action of benzyl benzoate is its relaxing effect upon spasms of smooth muscle tissue. The remedy was administered by mouth in doses of 25 minims of a 20 per cent. alcoholic solution—equivalent to 5 grains of the drug.

Vaccination by Subcutaneous Injection.—Goodall (*Lancet*, 1919, No. 5007, p. 285) has vaccinated hypodermically over 6000 men. He uses ordinary vaccine, injecting 1 c.c. for each inoculation. The local reaction usually is manifest within two to four days. It is variable in intensity, and was very mild except in a small percentage of cases. He compares the local reaction obtained with that following anti-typhoid inoculation; that is, local swelling, heat, tenderness. In those cases showing marked reaction, there was swelling of the entire arm and hand with axillary involvement. After the seventh to the tenth day, the local swelling and induration subsides leaving a hard nodule in the subcutaneous tissues. This nodule becomes well circumscribed and usually lasts for about one month. The general symptoms vary in intensity and are very similar to those of ordinary vaccination. Goodall claims that the advantages of this method are that it is a clean surgical operation and there is no open wound and therefore dressings are not required. He states that with proper technic the danger of secondary infection is practically eliminated. He claims that the percentage of positive reactions is very high; only 8 per cent. of vaccinations proved ineffective. This method is painless as compared with the ordinary method of scarification; it is for this reason that he believes it the best method of vaccinating children.

PEDIATRICS

UNDER THE CHARGE OF

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The Artificial Feeding of Athreptic Infants.—Marriott (*Arch. Ped. Proc. Sec. Dis. of Children, A.M.A.*, July, 1919) uses the term "athrepsia" in reference to that well known condition of extreme malnutrition known as marasmus or infantile atrophy. The condition of athrepsia is a condition of virtual starvation, in which the volume of the blood was diminished. This diminished flow of the blood was dependent in part at least upon a decreased blood volume, seemingly the result of a decreased protein content of the plasma and a consequent inability of the blood to maintain its water content. Very considerable amounts of food were indicated to meet this condition, yet the tolerance of many of these children for food was low and their digestion and absorption were necessarily poor. The tolerance of the infant for food might be increased by the use of gum acacia saline mixture intravenously. The problem remained of providing a food containing the elements essential to nutrition and which could be fed in large amounts without causing gastro-intestinal disturbances. In cases in which breast milk was not available, the use of lactic acid milk showed that it could be taken in larger quantities than sweet milk. Marriott came to regard buttermilk and protein milk as his chief reliance in feeding infants with gastro-intestinal disturbances. Fat-free lactic acid milk is low in caloric value. This might be increased by the

addition of sugar and starch, but even when enriched by sugar addition, it was not particularly adapted for the feeding of athreptic infants, particularly those under three months of age. There was no reason why the fat should all be removed from the lactic acid milk. In order to furnish the additional carbohydrate required by the athreptic infant, dextrins and glucose were added, the latter being absorbed with great rapidity. Glucose was very readily fermentable and for this reason was not used extensively in infant feeding. The dextrins, on the other hand, were not readily fermentable. It seemed that commercial glucose, being a mixture of dextrin, glucose and maltose might be suitable for the purpose. This is obtainable as corn syrup. Marriott added carbohydrate in the form of corn syrup to the whole lactic acid milk and used it in feeding athreptic infants. The results were as would have been expected. There was no tendency to diarrhea even when as much as 10 per cent. of the carbohydrate was added. There seemed to be almost no limit to the amount of carbohydrate that could be added to such a mixture. In addition a 5 per cent. solution might be given between feedings almost ad lib., as a means of supplying further calories. The thick syrup was rather inconvenient to handle, and could be best used in a solution containing 50 per cent. carbohydrate. As such a mixture was thick a nipple with a large hole had to be used in feeding. Up to the present time the author had fed forty infants varying in age from one and one-half months to eighteen months from periods of from four days to eight weeks. The amounts of carbohydrate added varied from 10 to 15 per cent. A gain in weight was noted in these children when a sufficient caloric intake was reached and generally continued steadily for days and weeks interrupted only by acute infections. Few infants, whose weight was as low as 50 per cent. of the normal weight for their age gained on less than 160 calories per kilo and many required 200 calories or more. The gain in weight in these infants was not due to a process of water logging. There was no tendency to edema and none of the excessive flabbiness observed in condensed milk babies. It might be noted that although the food described contained a high percentage of carbohydrates it was also high in protein and fat, the relative proportions being similar to those of ordinary milk mixtures. This mixture as described contained from 25 to 30 calories per ounce.

A Study of the Relationship of Convulsions in Infancy and Childhood to Epilepsy.—Morse (*Am. Jour. Dis. Children,* August, 1919) recalls in this article the discussion of twenty or twenty-five years ago as to the connection between the convulsions of infancy and early childhood to epilepsy. Since that time he has made observations of the babies and children with convulsions that he has seen in consultation and in private practice. He includes in his observations only those cases in which the convulsions were the primary cause for calling in a medical attendant and he excludes all those cases in which there is any evidence of acute or chronic cerebral disease. This study was conducted with two objects. The first was to determine what proportion of the children, otherwise apparently normal, having convulsions have epilepsy or develop it later. The second was to find out if possible whether there is anything in the history or in the manner of development of the convulsions to show whether or not they are manifestations of epilepsy, or whether

they will be followed by or develop epilepsy later. Satisfactory reports regarding 107 children was obtained. The time elapsed has varied from two to twenty years. In order to study these cases they were divided into four classes: (1) Those having convulsions associated with spasmophilia; (2) those cases in which the convulsions occurred in the course of whooping-cough; (3) those in which there was a single convulsion or a series of convulsions at the onset of some acute disease or with an attack of acute indigestion; (4) those in which there had been repeated convulsions during a considerable period or in which there had been repeated attacks suggesting petit mal. The results of this study were most unsatisfactory and very few conclusions could be drawn from it. Convulsions, which are manifestations of spasmophilia, are not likely to eventuate in epilepsy. Convulsions which occur in the course of whooping-cough must always be regarded as serious, as they are likely to be followed by epilepsy later. Single convulsions or a series of convulsions occurring at the onset of an acute disease or with an attack of acute indigestion are less likely to be followed by epilepsy than are repeated attacks during a considerable period or repeated attacks suggesting petit mal. Repeated attacks which would be classified as petit mal, or which suggest it, are just as likely to become epilepsy as repeated attacks of general convulsions. Nothing can be told from the nature of the early attacks as to the nature of the attacks when the epilepsy develops. When an injury to the head has directly preceded the onset of the attacks or there is no apparent cause for the attacks, epilepsy is more probable than when there is an apparent cause, such as indigestion, for each attack. The presence of an apparent cause for the attack does not, however, exclude epilepsy. The longer the attacks have persisted the more probable is the diagnosis of epilepsy. General impressions, which cannot be explained, have a certain value in diagnosis. Finally, and most positively, there is no way to determine immediately when a baby or a child has a convulsion, or has had repeated convulsions, or repeated attacks suggesting petit mal, whether it has epilepsy or whether it will develop it later.

A Study of the Lactose, Fat and Protein Content of Women's Milk.—Denis and Talbot (*Am. Jour. Dis. Children*, August, 1919) give the results of their investigations of the composition of human milk under different conditions. They point out the fact that, while the limits and variations in the fat and protein content of human milk are well established, a great deal of uncertainty exists as to the amount of lactose present. This is due to the fact that while reliable and simple methods for the determination of fat and protein have been in use for many years, the technic for sugar determination is still complicated. Recently newer methods have been promulgated for the determination of lactose. In addition there has been introduced another simpler method of fat and protein determination so that it is possible now to determine accurately the quantity of fat, protein or lactose from small samples of milk. It was found that there is a rapid increase of lactose during the first few days when colostrum changes into milk, and a further increase as lactation progresses. The reverse is true of protein which after the first rapid decrease during the change from colostrum to milk tends to further decrease during the course of lactation. After

the colostrum period there does not seem to be any relation between the stage of lactation and the amount of fat in the milk. There is usually a higher percentage of lactose at the beginning of a single nursing than at the end. Although this difference may be one or more per cent., it is usually higher at the end of nursing than at the beginning. There is very little, if any, difference in the protein. The milks taken simultaneously from both breasts of the same woman tend to have the same composition, but often vary in respect to the percentage of fat. Toward the middle of the afternoon or later the volume of milk in a woman tends to diminish. The percentage of fat is as a rule higher at mid-day or mid-afternoon than at other times of the day.

OBSTETRICS

UNDER THE CHARGE OF

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The Puerperal Period Complicated by Sloughing Fibroid.—KOSMAK (*Am. Jour. Obst.*, March, 1919) records the case of a primipara admitted to the hospital at term with a history of bleeding for a few days. On examination the cervix was soft and boggy, with two fingers' dilatation, the membranes intact and vertex presentation of the fetus without engagement. A low implantation of the placenta was made, but there was little bleeding and the general condition was good. Labor progressed very slowly and the dilating bag was introduced and spontaneous delivery occurred. There was moderate hemorrhage during the third stage. Lacerations were repaired. After the birth of the child the patient was irrational and very restless for several days, and a tumor the size of a fibroid head could be outlined on the anterior wall of the uterus. There was considerable shock, and stimulation was needed for several days. A tear in the perineum sloughed without an attempt at union. Involution was very imperfect and the lower abdomen was tender. The lochial discharge was foul, but drainage seemed to be good. On the ninth day postpartum blood examination showed marked anemia, with hemoglobin 38 per cent. On the thirteenth day the patient complained of severe pain in the left lumbar region. Three days later she suddenly showed signs of a general peritonitis. The lower portion of the abdomen, with the tumor, was exceedingly tender. The symptoms pointed to a sloughing fibroid, with possible perforation. On internal examination the cervix was partially closed; there was no bulging behind the uterus and a very slight serous discharge. There was severe abdominal pain and great restlessness. The condition was so bad that it was thought advisable to wait until the following day, hoping that stimulants would bring about improvement. When section was done, seropurulent fluid escaped from the peritoneal cavity. The omentum was adherent to the top of the uterus, which contained the tumor. Perforation had occurred at a number of points through which purulent matter was exuded. The condition in the abdomen was that of diffuse

septic infection. Hysterectomy was performed as rapidly as possible. A stump of the cervix was left in the lower angle of the abdominal wound. The peritoneal incision was closed except at the lower angle, where a strip of iodoform gauze was passed down into the cul-de-sac. The patient was difficult to manage, refusing food, irrational and developing incontinence of the bladder and rectum, with beginning bed-sores. These were treated most successfully by exposing the tissues about them to the sunlight daily for several hours. There was a profuse genital discharge which persisted for some time. Thrombophlebitis of the left leg developed, but the patient gradually recovered and left the hospital in very fair condition. Examination of the material removed showed infection with the Bacillus coli communis. In discussing this paper several cases were reported of fatalities complicating pregnancy in which infection and sloughing developed. These cases were saved by hysterectomy, but it was thought that the operation should be done as early as possible.

The Technic of Salpingectomy in Ectopic Gestation.—CAREY (*Am. Jour. Obst.*, March, 1919) reports the case of a patient, aged thirty-nine years, admitted to the hospital with symptoms of ruptured ectopic pregnancy. At operation the left broad ligament was very much swollen, edematous and friable, and the tube was in the same condition. Abortion had taken place from the fimbriated end of the tube. The operator attempted to save a part of the tube and removed the outer half, leaving the ovary. After the patient's recovery she came for examination, when it was found there was a small, fixed, moderately tender mass on the left side of the uterus. The patient had a retroverted, prolapsed uterus, with old lacerations and cystocele, and on opening the abdomen the sigmoid and omentum were adherent in the region of the left tube and ovary, the part of the tube which had been left was atrophic and closed and the ovary had been replaced by a cyst a little larger than a golf-ball. The cyst was removed, the raw surface covered over and the uterus fixed to the anterior abdominal wall. The patient made a good recovery. The writer cites this case as illustrating the failure of his attempt to preserve a portion of the tube. He believes that a much better result would have been obtained had both tube and ovary been removed entire.

Contra-indications to the Use of Dilating Bags.—HULL (*Am. Jour. Obst.*, March, 1919) calls attention to several important contra-indications to the use of dilating bags. Before introducing the bag the operator should be sure that the cervix can be dilated and that there is good reason for believing that labor pains will develop. He must be on his guard against a rigid cervix and primary uterine inertia. In two cases the use of bags failed, although continuous traction was made with a two-pound weight. It was necessary to deliver these patients by vaginal Cesarean section. Bags were also contra-indicated when great haste is necessary, as in severe accidental hemorrhage, threatened edema of the lungs and tightly contracted uterus or failure in cardiac compensation. In contracted pelvis with a true conjugate of less than 8 cm. the use of bags should not be permitted. In borderland cases induction of labor has been abandoned by the writer. He prefers to put the patient in the best possible condition and to give her the trial of labor,

watching closely the condition of mother and child. The results of induced labor in contracted pelvis are so much inferior to those of spontaneous labor or Cesarean section that induced labor should rarely be done. In complete placenta previa with viable child, section should be employed instead of the use of the bag. Virulent infection of the genital organs should contra-indicate the use of the bag. As regards normal cases at term it is difficult to find a good excuse for interference by the use of dilating bags. There is no way of determining the proper time for this operation. and the complications which may accompany the use of bags are sufficiently important to be avoided. When dystocia lies in the soft parts it is often preached that the bag is the ideal method of treatment. It is true that complete dilatation cannot be obtained, for the bag cannot imitate or set up the normal action of the uterus. The cervix is never completely dilated under the use of the bag alone. While it is true there are certain conditions in which the bag acts properly, its use has been greatly overdone, and it does not give the best results in many cases.

Cerebral Hemorrhage Complicating Pregnancy.—LANGROCK (*Am. Jour. Obst.*, March, 1919) describes the case of a primipara, aged twenty-three years, who had been feeling well until she had a convulsion and became unconscious, and up to the time of her admission to the hospital did not regain consciousness. The diagnosis of eclampsia had been made, and on admission the blood-pressure was 180 and the pulse 54. The patient had Cheyne-Stokes breathing and the respirations were very shallow. Only a few drops of highly colored urine were obtained by catheter. There was slight edema of the lungs, more marked of the ankles. The whole right side of the body was exceedingly spastic, and this was also true of the left lower extremity. The neck was slightly rigid, the left pupil widely dilated, the right contracted to a pin-point and neither reacted to light, nor was there corneal reflex. Babinski's sign was present on both sides, with exaggerated knee-jerks. There were moist rales through the lungs, while the heart sounds were feeble and very irregular. On abdominal examination the uterus was eight and one-half months; the head was freely movable above the pelvis. The fetal heart was heard very plainly in the left lower quadrant, beating 148 times to the minute. On vaginal examination the cervix admitted two fingers, and was soft and thin. Lumbar puncture was exceedingly difficult and only a few cubic centimeters of bloody fluid was obtained. The patient was not in labor, although the cervix showed two fingers' dilatation and was soft and thin. The diagnosis lay between eclampsia and intracranial pressure, and the latter seemed probable because of the unequal pupils, which did not react; slow pulse, Cheyne-Stokes breathing, spastic contraction of muscles and the Babinski reflex. The intracranial pressure was thought to be due to cerebral hemorrhage from eclampsia, injury to the cranium during her fall to the floor following the first convulsion or cerebral hemorrhage from a rupture of the bloodvessel, the seat of syphilitic endarteritis. At the moment of the patient's death, postmortem Cesarean section was done, and a child weighing six pounds and fourteen ounces, vigorous and in good condition, was delivered. The patient lived but a short time, dying from failure of the action of the heart, with profound cyanosis.

GYNECOLOGY

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Carcinoma of Ovarian Teratoma.—In view of the evident irritating character of the contained cyst fluid, together with the chronic irritation caused by the hair, producing as it does granulation tissue with giant-cell formation, it is remarkable that more cases of carcinomatous degeneration of the epithelial lining of teratomatous cysts, commonly called "dermoid cysts," of the ovary have not been observed. A possibility exists that too often these tumors are regarded as innocent and no gross or microscopic examination of the tumor is made as a matter of routine. In view of the skepticism usually expressed in commenting on carcinoma of the ovary arising from the epithelial lining of a cystic teratoma, the case recently reported by SPALDING (*Am. Jour. Obst.*, 1919, lxxx, 401) is of more than passing interest. The tumor was noted some days after operation following the laboratory routine which has to do with more pathology than the staff can promptly handle. It has taught the lesson, however, to cut all tumors grossly in the operating room and to have frozen sections made in suspicious cases before the abdomen is closed. In this case the tumor that was removed had all the appearances of an ordinary dermoid cyst, containing gelatinous fluid and red hair, but in addition there was a small nodule, yellow in color, which was resting on the cyst lining and which was surrounded by a narrow margin of ovarian tissue. Microscopic examination of this nodule showed a thin stratum of pavement epithelium with a distinct basement-cell layer. This epithelial layer varies in thickness and at one point gives the appearance of malignant change. The epithelial cells are increased in number at this point forming a small epithelial pearl which seems to be breaking through the basement-cell layer to invade the deeper tissues. Immediately beneath the epithelium is a layer of connective tissue and muscle cells which contain many sebaceous glands and several hair follicles. Several of these glands are invaded with epithelial cell masses resembling basal-cell carcinoma. Intermingled with the deeper layers of the connective tissue and extending to the fibrous capsule of the teratoma but not penetrating it is a carcinomatous mass forming in part solid masses of small, round epithelial cells surrounded by a scanty amount of connective tissue and in part small collections of epithelial cells having an alveolar arrangement. From this pathological picture it is very difficult to decide whether the process is an adenocarcinoma or a basement-cell carcinoma and whether the malignant tumor is primarily in the ovary or comes from a malignant

degeneration of the epithelial lining of the teratoma. In the year and a half that has elapsed since operation there has been no evidence of a recurrence, a fact uniquely at variance with the heretofore reported cases. This suggests the possibility that with early carcinoma the prognosis may be good because of the thick protecting capsule of the teratoma.

Secondary Syphilis of the Uterus.—Secondary syphilis of the uterus is seldom recognized and in the few cases that have been reported, the lesions have consisted of macules, papules and ulcerations located on the outside of the cervix. In a most interesting case reported by GELLHORN (*Surg., Gynec. and Obst.*, 1919, xxix, 374) the signs differed from this general picture in several important particulars. Whereas in all previously known cases the lesion was situated upon the outside of the vaginal portion, this is probably the first instance where the specific affection could be demonstrated within the cervical canal. This was possible because there was a marked eversion of the cervix which exposed the lower third of the cervical canal. The cervical mucosa showed posteriorly, an oblong patch, about $\frac{3}{4}$ cm. in its longest diameter, which lay about $\frac{1}{2}$ cm. from the external os. This patch was very slightly raised above the neighboring mucosa and had a finely granular, pinkish surface. At the circumference and extending a little into the patch was a faintly yellowish discoloration. Two other smaller and more nearly round patches lay to the right of the larger lesion, and a fourth patch could be seen upon the mucosa anteriorly. All these patches felt soft to the touch and bled very slightly when rubbed with a cotton-armored applicator. The secretions from these patches showed an abundance of very active spirochetes of the typical pallida variety. There were no secondary lesions anywhere on the body, and as the state of the primary lesion on the labium minus indicated the recent date of the infection, the intracervical ulcerations must be regarded as the first and only secondary manifestations of syphilis in this patient. Another important point that has been brought forward by this case has to do with the heretofore accepted view that the normal secretions of syphilitic women may cause infection even in the absence of local specific manifestations. In the light of the present observation, however, this conclusion may have to be modified, since the fortunate coincidence of a cervical tear permitted Gellhorn to inspect the inside of the cervical canal and to find there the specific lesions with their rich supply of spirochetes. It is permissible to assume that in all the previously reported cases in which syphilis was transmitted in the absence of any apparent lesions in the vagina or on the cervix, that such lesions existed within the cervical canal but were invisible through the closed external os. Until further evidence to the contrary is obtained, it will be safe to adhere to the old view that discharges contain spirochetes only in the presence of a local lesion.

Operation for Hypertrophic Elongation of the Cervix.—The operative procedure that has been suggested by NOBLE (*Am. Jour. Obst.*, 1919, lxxx, 409) for the correction of that interesting condition known as hypertrophic elongation of the cervix uteri, consists of resection of the

middle portion of the cervix supplemented by a shortening of the utero-sacral ligaments by way of the vagina. The incision is made in the anterior median line of the vagina after the manner of a vaginal hysterectomy except that in place of encircling the cervix, the ends of the "Y" terminate at the side of the portio vaginalis. The bladder is liberated from the trigonum to the uterovesical peritoneum and laterally the dissection is extended outward along the base of the broad ligament to the ureter on either side and the peritoneum of Douglas's pouch is stripped free from the cervix up to the internal os. After liberating the neck of the uterus it is detached from the vagina by a V-shaped incision cutting from either side downward and toward the axis of the cervical canal. The incision should be made low enough to place the apex of the V at the vaginal junction. The resection is then completed by a similar incision immediately below the internal os, the effect of which produces a wedge-shaped stump of the uterus which will fit over the remaining cervical stump. At this point, the finger is passed into Douglas's pouch to locate the uterosacral ligament on the patient's left. Should it be completely effaced its markings may be located by drawing the uterus downward when a fold may be felt extending from the cervicocorporeal junction to the sacrum. With a pair of curved artery forceps thrust through the base of the broad ligament in the space between the uterus and the ureter (below the uterine artery) the fold or ligament is drawn well into the vagina and temporarily secured by a retention suture. The ligament on the opposite side is secured in like manner. Following this step the wedge stump of the uterus is secured in the V of the vaginal stump, first introducing a forceps or similar instrument through the vaginal portion and into the cavity of the uterus. Upon such an instrument the two sections are brought together and secured by a mattress suture of kangaroo tendon on either side, the two sections practically "dovetailing" into one another. To maintain perfect alignment of the canal a suture of catgut fixes the tip of the wedge into the angle of the V. By pulling upon the temporary retention sutures attached to the uterosacral ligaments, the latter will be drawn into the denuded field and tracing them step by step, using one pair of forceps after another, they may be brought far enough into the vagina to be sutured together in front of the cervix, the latter being forced well back into the hollow of the sacrum to secure normal fixation of the lower pole of the uterus. The excess of the vaginal flaps is then trimmed away and the vagina is closed with kangaroo tendon, the lower angles of the incision being left open for drainage. The edema of the vaginal portion which follows commonly disappears without attention but when the hypertrophy is due to inflammatory changes, wedge-shaped sections of anterior and posterior lips may be removed with good effect. On account of the relaxation of the vagina and its outlet, posterior colporrhaphy with especial attention to constructive reinforcement of the perineum is essential to effective employment of the mechanical principles involved in the technic of the operation.

OPHTHALMOLOGY

UNDER THE CHARGE OF
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Detachment of Retina in Toxemia of Pregnancy.—CLAPP (*Am. Jour. Ophthal.*, July, 1919, p. 473) has examined the eyes of practically all of the albuminuria and toxemia cases occurring in the past fourteen years at the Maryland Lying-in Hospital, and has not observed detachment of the retina until recently. Six cases have presented themselves since December, 1917, whose histories are briefly detailed. They varied in extent from small to almost complete detachment of the retina, in contradistinction to so-called idiopathic detachments, these have all subsided and become reattached with normal fields of vision. They may be antepartum or postpartum, and may clear up in a few hours, and are frequently far forward in the periphery and found only after some searching. They are probably present much more frequently than heretofore recorded and the prognosis is good so far as the detachment is concerned.

The Eye of Birds.—ROCHON-DUVIGNEAUD (*Annal. d'oculist.*, June, 1919, p. 376) gives a résumé of the anatomy of the eye of birds. There are two types of eyes in birds: that of the diurnal with small cornea and large posterior segment, and that of the nocturnal with large cornea (and large crystalline) and relatively small posterior segment. The eye of diving birds presents certain peculiarities at the sclero-corneal limbus: a kind of circular dilatation entirely surrounding the cornea. The crystalline of birds shows as its most important peculiarity an annular collar, the greater or less development of which according to different species modifies the form and consequently the refraction of the lens. The vitreous of birds is very consistent, which coupled with the bony scleral ring and the cartilaginous plate lining the entire sclerotic results in the posterior segment being very resistant, so that it is little or not at all affected by modifications of tension: the latter involves only the anterior chamber, very deep in the diurnal, still deeper in the nocturnal; the aqueous humor accordingly plays the essential part in the physiological maintenance and modifications of the intra-ocular tension. The pecten is nothing but a vascular membrane derived from the optic nerve, of which it represents the capillary network as a forward extension. It is an organ of nutrition to compensate the complete avascularity of the bird's retina; it has nothing to do with the accommodation. It is relegated to the postero-inferior segment of the eye, below and behind the foveal region so as not to interfere with the function of the latter. It is smaller in the nocturnal, probably because

the retina of these birds is relatively smaller than that of the diurnal. The ciliary muscle consists of three systems of striated fibers, the mechanism of which is incomprehensible with present theories of accommodation. The raptores, eagle, hawk, etc., possess actually two foveæ, one central, the other further back (fovea lateralis). The central fovea is the principal one; its cellular layers (particularly the bipolar cells) are richer in elements. The posterior fovea is, however, well marked as a fovea: it is more or less developed according to the species. The eye of the eagle presents no difference, compared with that of other diurnal raptores except perhaps greater thickness of the osseous scleral plaques. Its axis is 27 mm. long with a maximum width of 32 mm.: it is accordingly larger and longer than the human eye; the retinal images of the eagle are therefore much larger than those of man—a circumstance favorable for visual acuity independent of all special function of the retina.

PATHOLOGY AND BACTERIOLOGY

UNDER THE CHARGE OF

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The Occurrence of Bacillus Influenzæ in the Normal Throat.—During the epidemic of influenza in October, 1918, PRITCHETT and STILLMAN found this organism present in 42 per cent. of 177 healthy individuals from whom no history or respiratory infection was obtainable. These observers found the same organism in the throats of convalescents from influenza in 46 per cent. of individuals studied. In the same epidemic period Lord, Scott and Nye demonstrated B. influenzæ in the pharyngeal secretions of 76 per cent. of 34 healthy men of the Harvard S. A. T. C. Opie and his collaborators found B. influenzæ in the mouths of 35.1 per cent. of all healthy men examined at Camp Funston. These figures indicate the wide distribution and prevalence of the organism during the severe epidemic of this acute respiratory disease. The authors (*Jour. Exper. Med.*, 1919, xxx, 497) made a study of the personnel of the Rockefeller Institute. Following up the examinations reported in their previous paper they have been able to make repeated cultural examinations of the throats of 84 of the same persons during a period of six months. The present study indicates that the percentage incidence of those haboring B. influenzæ in the upper respiratory tract is as great during the post-epidemic period as it was during the influenza epidemic. From December, 1918, to June, 1919, the percentage of carriers in a group of 150 individuals has averaged 41 per cent. per month. This percentage incidence of healthy persons found to harbor influenza bacilli in their throats and saliva is approximately the same as that recorded by Pritchett and Stillman during the height of the epidemic. In addition it is of interest that in a boys' orphan asylum in which no case of influenza had occurred during

the epidemic 39 per cent. of throat cultures taken from 190 boys showed the presence of B. influenzæ. This percentage incidence of positive cultures is the same as that found in the examination of 52 convalescents from influenza in an institution for girls in which over half the personnel had suffered from the disease. Healthy persons have been found to have positive throat cultures for a considerable period of time, in six instances during five months and in thirteen instances during a period of four months. The authors in every case used Avery's oleate hemoglobin agar. The optimum hydrogen ion concentration for this medium is shown to lie between pH 7.2 and 7.5. Any variation beyond this range, particularly on the alkaline side, reduces markedly the suitability of this medium for growth of Bacillus influenzæ. Oleate hemoglobin agar not only enhances the growth of the influenza bacillus, but by inhibiting the growth of other organisms, such as streptococci and pneumococci, greatly facilitates the isolation of Bacillus influenzæ from a focus which harbors a wide variety of other bacteria.

The Relationship of Proteolytic Enzymes in the Pneumonic Lung to Hydrogen Ion Concentration. An Explanation of Resolution.—LARD (*Jour. Exper. Med.*, 1919, xxx, 379) studied the effect of varying hydrogen ion concentration on the proteolytic activity of the cellular material of pneumonic lungs. This cellular material was the washed filtrate of finely ground lungs in the stage of grayish-red or gray hepatization and consisted mainly of pus cells, large mononuclear cells and pneumococci. In this he found evidence of the presence of a proteolytic enzyme which digested coagulated serum (Loeffler's blood serum, at a hydrogen ion concentration of pH 7.3 to pH 6.7). This enzyme was inactive at higher hydrogen ion concentrations. The pneumococci in the material had been killed by addition of chloroform. Also there was the presence of a proteolytic enzyme which was active between hydrogen ion concentration of pH 8 to pH 4.8. This was most active, however, at pH 6.3 to pH 5.2. He suggests that this enzyme action may be responsible for the dissolving of the exudate at resolution, *i. e.*, as a gradual increase in acidity occurs in the diseased lung the enzyme operative between pH 7.8 and pH 6.7 breaks down the fibrin. When a pH 6.7 is reached its action probably ceases and the action of the second enzymes continues, becoming very active between pH 6.3 and pH 5.2 splitting the peptones to amino-acid nitrogen.

Relations Between Pneumococci and Hydrogen Ion Concentration.—AVERY and CULLEN (*Jour. Exper. Med.*, 1919, xxx, 359) studied the hydrogen ion concentration at which bacterial growth of the various immunological types ceased, in an effort to determine if this method could be used for type determination. They obtained unsatisfactory results. Growth ceased with all types when a final hydrogen ion concentration of about pH 5 had been reached if sufficient fermentable carbohydrate was present in the culture media. Using dextrose this was found to be above 0.4 per cent. The same results were obtained using maltose, saccharose, lactose, galactose, raffinose and inulin. Excess of carbohydrate in the media up to 4 per cent. as tested did not influence this final reaction. They confirmed the results of Dernby and Avery, that the optimum hydrogen ion concentration for growth

of the pneumococcus is pH 7.8. Where no carbohydrate was present other than that extracted from the meat as in plain broth, growth initiated at the optimum reaction of pH 7.8 ceased at about pH 7. If bacteria-free filtrates of such plain broth cultures were again readjusted to pH 7.8 and reinoculated the pneumococci could not grow unless carbohydrates were added. With such filtrates of dextrose broth cultures which had reached a final reaction, pH 5, growth occurred upon readjustment to pH 7.8 and reinoculation. Apparently one of the factors necessary for the growth of the pneumococcus is the presence of a certain amount of fermentable carbohydrate. LORD and NYE (*Jour. Exper. Med.*, 1919, xxx, 389) also found the final hydrogen ion concentration for growth of the pneumococcus to be about pH 5. There were no noteworthy differences with the various immunological types except in one instance when a strain of type I pneumococci remained alive for ten days after a hydrogen ion concentration in the culture media of pH 4.5 had been reached. They also found growth in dextrose broth cultures which had reached the final hydrogen ion concentration after readjusting the reaction and reinoculating. The strains of pneumococci tested withstood a hydrogen ion concentration of pH 5.3, one hour; pH 5.6, three hours; and pH 6.1, six hours before death of the organisms occurred. Cloudy suspensions of washed living pneumococci incubated with equal quantities of standard solutions of varying hydrogen ion concentration showed that there was no growth of the bacteria in tubes of pH 5.6 or higher concentrations after five and a half hours. In some of the tubes a clearing occurred due to dissolution or disintegration of the bacteria after seven hours. This was complete in such tubes of pH 5 to pH 6 only, the tubes on the more acid side remaining cloudy. There was constantly some clearing on the more alkaline side of the scale. They conjecture from this that the dissolution is not due to acidity alone as the more acid side of the scale remained cloudy and suggest that an enzyme derived from the pneumococci themselves active at pH 5 to pH 6 may be responsible. From these two studies it seems certain that fermentable carbohydrate must be present for the growth of pneumococci and that where this is present the production of acid is the most important bactericidal factor.

Experimental Streptococcic Tonsillitis.—In an attempt to ascertain the mode of dissemination and cause of influenza by the transference of secretions from the upper respiratory passage of influenza cases, to the nose and throat of healthy volunteer individuals, RICHEY (*Jour. Infect. Dis.*, 1919, xxv, 299) reports the production of tonsillitis in sixteen of 155 individuals who submitted themselves for the experimentation. Crude, unfiltered nasopharyngeal washings and bronchial secretions from acute typical cases of influenza were instilled into the nasopharynx of each volunteer. The usual incubation period was thirty-six to seventy-two hours. The predominating organisms in cultures from tonsils in early stages of the illness were hemolytic streptococci. Three of these cases had received one month previously a vaccine consisting of Bacillus influenza, pneumococcus, types I, II and III and Streptococcus hemolyticus in presumably adequate doses. A review of streptococcus vaccine therapy is given.

HYGIENE AND PUBLIC HEALTH

UNDER THE CHARGE OF

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Observations on the Food of Anopheles Larvæ.—METZ (*Public Health Reports*, 1919, xxxiv, 1790) concludes an experimental study of the subject with the following discussion: It is evident from these experiments that the diet of Anopheles larvæ may be either heterogeneous or homogeneous—consisting of mixed animal and vegetable materials, of mixed vegetable materials or of individual species of plants or animals. And, apparently, it makes little difference whether the food is composed of living organisms or their dead remains. No effort was made to ascertain how many types of plants and animals furnish suitable food materials, since the range is evidently great. Only one of the types tested gave indications of being unsuited. This was Chara, and even it provided adequate food for the development of some larvæ to maturity. Of greater interest, perhaps, is the evidence regarding the effect of pollution or decomposition on the larval development. In most of the above experiments the culture media in which the Anopheles larvæ developed were essentially sterile, *i. e.*, there were practically no protozoa present and there was a negligible amount of bacterial action. The cultures were kept in shallow granite pans, 10 to 12 inches in diameter and 3 inches deep, and it was found that no artificial aëration was necessary. In other cases, when cultures containing relatively large amounts of decomposing vegetation were brought into the laboratory and kept without sterilization or aëration, the larvæ usually lost vigor and died in a few days. Thus the experimental evidence leaves little doubt as to the detrimental effects of pollution or decomposition. Whether the injurious effects of decomposition are due directly to bacterial or protozoal action on the larvæ themselves or indirectly to an excess of CO_2 or other gases resulting from the decomposition is not certain. The latter seems more probable, however, since the detrimental effects may often be prevented by aëration. Contrary to popular belief, then, it appears that the purer and more sterile the waters may be, so long as they contain sufficient food, the more suitable they are for Anopheles breeding. This would seem to account for the fact that rain-water puddles and seepage pools frequently permit much more prolific breeding than near-by, stagnant waters. It also serves to emphasize the danger of doing more harm than good by cleaning the refuse from such places as sloughs and stagnant puddles, unless adequate provision is made for subsequent drainage, oiling, fish control or some other method of mosquito eradication.

Observations on the Bacteriology of Influenza.—JORDAN (*Public Health Reports*, 1919, xxxiv, 1413) studied several groups of cases of influenza and other respiratory affections, with the object of ascertaining the frequency of Pfeiffer's bacillus, the Mather's diplostreptococcus and variations in bacterial flora throughout the illness. It was found that by ordinary bacteriological methods the flora varied markedly and that individuals of groups coming in intimate contact tend to a more or less uniform flora. In influenza Pfeiffer's bacillus and Mather's coccus occurred with greater frequency than other pathogenic organisms, and of the two mentioned Mather's organism seemed to be more frequently associated with pneumonia. In colds Pfeiffer's bacillus was relatively infrequent while Mather's coccus was present about as often as in influenza, and the latter organism was present in colds and rhinitis about as often as in influenza. Hemolytic streptococci appeared to be associated with tonsillitis and severe throat inflammation, while this organism was relatively rare in influenza. In the observations on "recurrences" of influenza, organisms different from those in the original attack were observed, and the opinion is expressed that "second attacks" are due to organisms different from those etiologically related to the first one.

Occurrence of Bacillus Botulinus in Nature.—BURKE (*Jour. Bacteriol.*, 1919, iv, 541) made 235 cultures from samples collected in five localities in central California, fifty or more miles distant from each other. The cultures covered a wide range of material, including tap water, hay, leaves, vegetables and fruits in various conditions, insects, spiders, sow bugs, snails, and caterpillars, garden soil, manure from horses, hogs, and chickens and also samples from the claws and beaks, and crop gizzard and intestinal contents of birds. Seven cultures of Bacillus botulinus were found in bruised and moldy cherries, bird-pecked cherries, pole bean leaf covered with spots or droppings of insects or small animals, spiders from bush bean plants, bush beans, some of which were slightly scarred, picked over, washed and packed in clean jars for canning, manure from large hog which had recovered from botulism three months before sample was taken, and discolored moldy hay from an outdoor stack. Four cultures were found in which there was evidence of toxin, but it was so weak that the toxin-antitoxin tests were not considered reliable. This material was obtained from earth from spider tube, spider droppings and web, sow bug from bush bean plant, linnet claws, spider and small bugs from bush beans. Burke therefore concludes that Bacillus botulinus is widely distributed in nature, and that it is present in the garden and may be on the fruit or vegetables when they are picked. Bacillus botulinus is not necessarily associated with active decay. It may be present in the blemishes or spots on the skin of apparently sound fruit and vegetables. Bacillus botulinus may remain in the intestinal tract of an animal for at least four months after contaminated food has been eaten. Bacillus botulinus may not occur far from the habitation of man. Of the five localities visited, only one failed to give positive results as to the presence of Bacillus botulinus. There were no human beings living on the place, no domestic animals other than horses, and there was no vegetable garden. Bacillus botulinus may be closely associated with or dis-

seminated by spiders or insects common in gardens in California. Since Bacillus botulinus grows readily at temperatures as low as 22° C., there is no reason for assuming that this organism must be associated with the stools of warm-blooded animals.

The Diagnosis of Rabies in Animals.—HASSELTINE (*Public Health Reports*, 1919, xxxiv, 2378) describes his work and summarizes it as follows: The time required for the performance of the different tests is approximately as follows: Smear test: One hour (frequently less) after arrival of specimen. Section test: Three to four days (a hurried test can be done in a day but will usually be unsatisfactory). Animal inoculation test: Ten days to six months. After thirty days the probability of a positive result is small. In conclusion, therefore, it may be stated that, based on 1003 specimens examined, the correct diagnosis may be obtained on the day of receipt of specimen in 90 per cent. of the cases; within five days, in about 92 per cent.; and at the end of one month practically all will be determined. Hence a negative report on microscopic examination with subsequent inoculation of animals practically becomes a confirmed negative at the end of one month, though it is the rule at present to observe animals for six months.

Malaria in England in 1917 and 1918.—CARTER, of the U. S. Public Health Service (*Public Health Reports*, 1919, vol. xxxiv) reviews the recent outbreaks of malaria in England caused by the repatriation of large numbers of parasite-infected soldiers and emphasizes the unfavorable nature of the environment by pointing out that 15,000 imported cases gave rise to not more than 326 cases. The relatively small number of the mosquito hosts account for the failure of the disease to spread, though apparently the hosts are numerous enough to keep alive a small amount of infection even under ordinary conditions. It is predicted that the imported malaria will be of no importance in a year or two.

The Felix-Weil Reaction as a Laboratory Test in the Diagnosis of Typhus Fever.—BENGTSON (*Public Health Reports*, 1919, xxxiv, 2446) describes a relatively new diagnostic test for typhus fever. It depends on the agglutination of certain members of the proteus group with the serum from typhus cases. The method seems to be comparable with the Widal reaction in availability and it is in fairly general use where typhus prevails. The reaction appears in the first week of illness but is higher during the second week and during convalescence. A single positive result with a case of typhus of American origin is reported.

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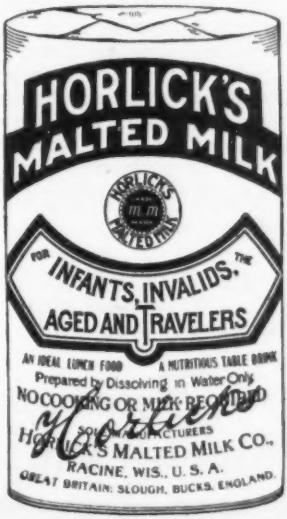
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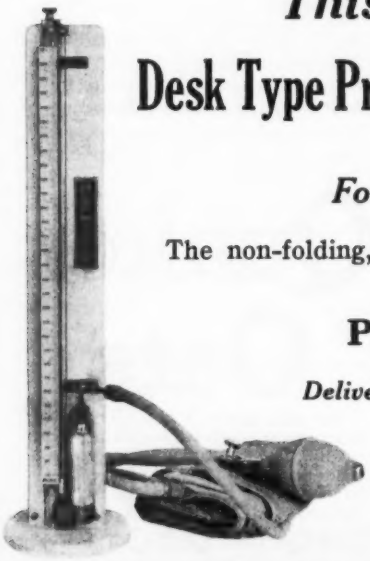

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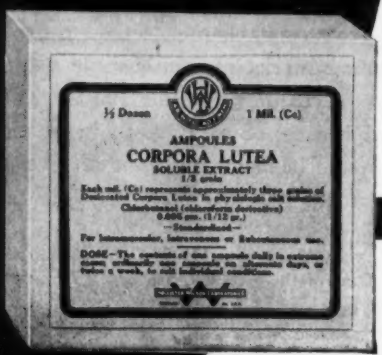

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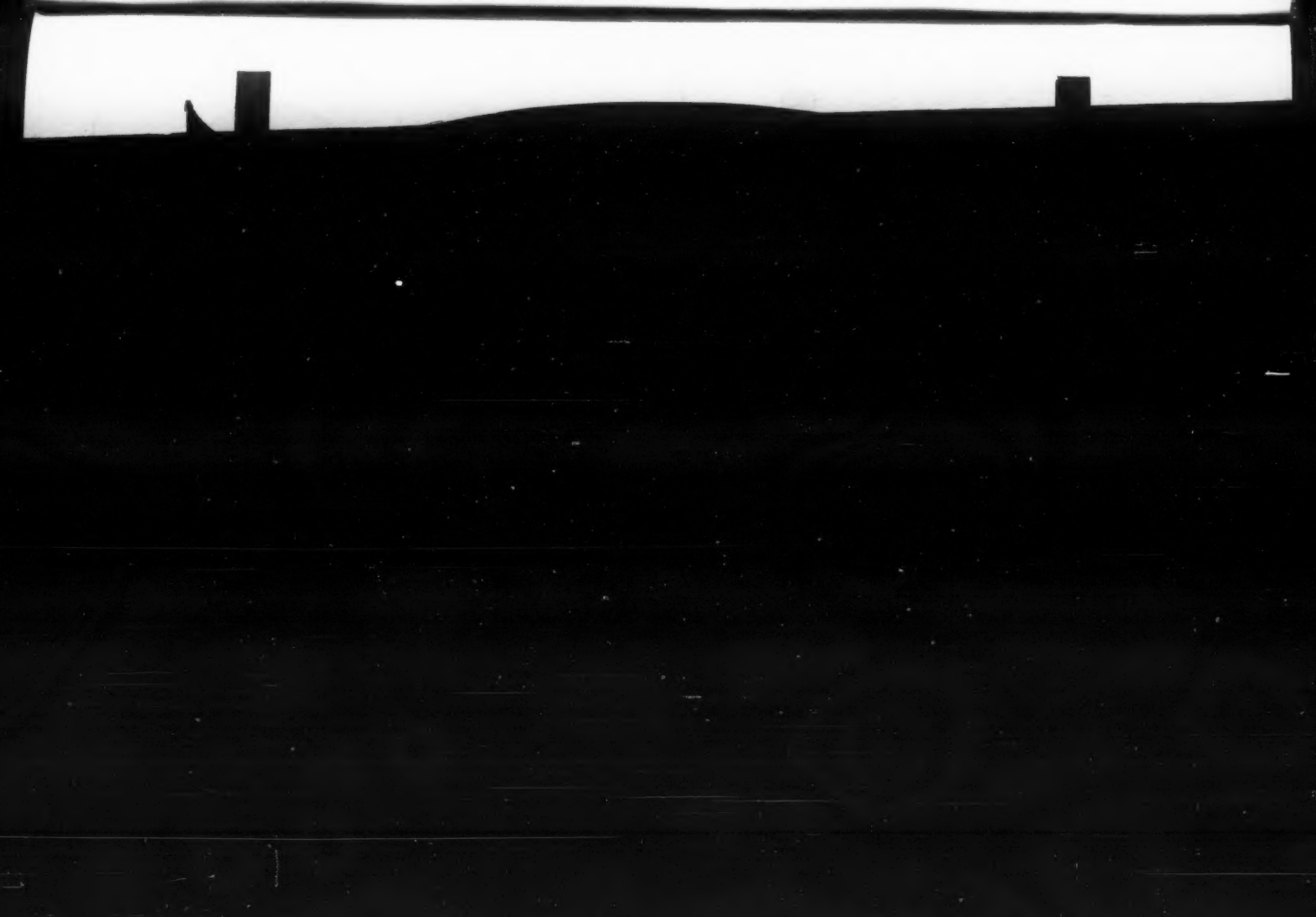

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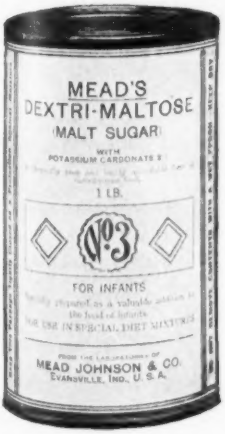

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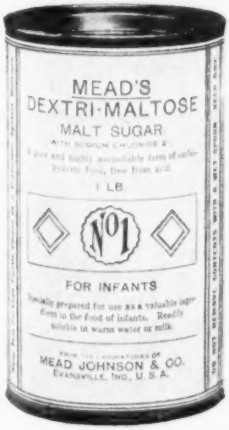

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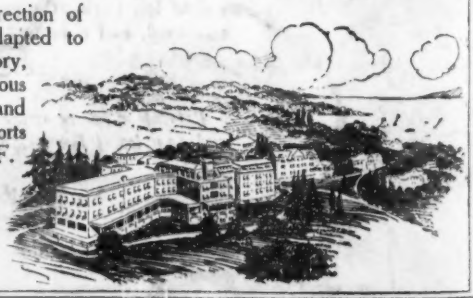
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